Exhibit 27

INTERAGENCY WORKING GROUP ON ASBESTOS IN CONSUMER PRODUCTS (IWGACP)

Appendices to White Paper: IWGACP Scientific Opinions on Testing Methods for Asbestos in Cosmetic Products Containing Talc[a]

[a] Including talc intended for use in cosmetics

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APPENDIX A: PURPOSE AND FORMATION OF IWGACP

1. IWGACP Formation and Membership

In October 2018, the U.S. Food and Drug Administration (FDA) formed the Interagency Working Group on Asbestos in Consumer Products (IWGACP), as a result of concerns regarding the presence of asbestos in talc-containing cosmetic products and following several recalls of cosmetic products[1] by retailers in the US and globally (Canada, Netherlands, Taiwan)[2]. Originally composed of subject matter experts (SMEs) from eight federal agencies[3], this working group was asked to develop a consensus document with recommendations that could be potentially used for regulatory policy development to support improved testing methods for asbestos and other mineral particles of concern that could potentially affect consumer product safety. The IWGACP was specifically tasked to address terminology and definitions of asbestos and other particles of health concern in talc[4] and talc-containing consumer products, recommend methodological improvements for measuring asbestos in talc and talc-containing consumer products, and recommend laboratory reporting standards for testing talc and talc-containing consumer products. Although the original scope of the IWGACP was consumer products that contain talc, in early 2020 the scope was narrowed to talc intended for use in cosmetics and talc-containing cosmetic products.

The FDA Office of Cosmetics and Colors (OCAC) in the Center for Food Safety and Applied Nutrition (CFSAN) organized and managed the IWGACP since many talc-containing products are cosmetics. Because >90% of talc [Bolen (USGS) 2020] and all asbestos in the US market is used to manufacture products that are not regulated by FDA, other federal agencies were asked to provide SMEs having experience and expertise related to talc geology, mineralogy, and toxicology, in addition to asbestos-testing methodologies and regulation. The IWGACP originally consisted of 38 SMEs from the eight participating federal agencies. These SMEs did

[1] https://www.fda.gov/cosmetics/cosmetics-recalls-alerts/fda-advises-consumers-stop-using-certain-cosmetic-products; https://www.fda.gov/news-events/press-announcements/statement-fda-commissioner-scott-gottlieb-md-and-susan-mayne-phd-director-center-food-safety-and.

[2] Other countries' regulatory bodies, including Health Canada (https://healthycanadians.gc.ca/recall-alert-rappel-avis/hc-sc/2019/69454r-eng.php); the Dutch Food Safety Authority (Nederlandse Voedsel- en Warenautoriteit; https://www.ilent.nl/documenten/publicaties/2018/03/28/rapportage-twee-op-asbest-geteste-producten), and Taiwan's FDA (https://focustaiwan.tw/society/201907270005) have also detected asbestos in the same cosmetic brands and have issued product recalls.

[3] The eight original federal agencies include: FDA, National Institute for Occupational Safety and Health (NIOSH), National Institute of Health (NIH)/National Institute of Environmental Health Sciences (NIEHS), Occupational Safety and Health Administration (OSHA), Environmental Protection Agency (EPA), Consumer Product Safety Commission (CPSC), U.S. Geological Survey (USGS) and the National Institute of Standards & Technology (NIST). In mid-2020, the NIST SME retired without a replacement, and in November 2020, the OSHA representatives ceased active participation, bringing the current number of participating agencies to six.

[4] Unless otherwise specified, references to testing of talc in this document are to talc intended for use in cosmetics.

not represent or speak for their respective agencies, except to provide an understanding of how federal agencies arrived at their respective policies and/or regulations. Discussions were focused on the unique perspectives that each member, as a scientist, gained through addressing issues involving asbestos testing while working for his or her federal agency or in a similar capacity as a scientist/researcher.

This White Paper reflects more than two years of deliberations and the current thinking of the IWGACP SMEs. The IWGACP scientific opinions are intended to inform FDA's consideration of testing methods for talc-containing cosmetics and talc intended for use in cosmetics. These scientific opinions and related advice do not represent recommendations or policies of the FDA or any other federal agency, or proposed changes to any regulations of the U.S. Government. None of the scientific opinions of the IWGACP and this White Paper should be construed as an endorsement or change in policy of any US government agency.

2. Joint Institute for Food Safety and Applied Nutrition (JIFSAN) Symposium

On November 28, 2018, JIFSAN[5] convened a symposium, titled "Asbestos in Talc"[6] to provide a forum for experts in asbestos mineral analysis, from industry, academics, and government, to share knowledge and experience regarding testing methods for the analysis of talc, criteria used for mineral particle identification, and data interpretation. JIFSAN is a multidisciplinary research, education, and outreach program, jointly administered by the FDA and the University of Maryland, that provides scientific expertise for ensuring a safe, wholesome food supply, as well as the infrastructure for contributions to national food safety programs and international food standards. Many of the IWGACP SMEs attended the JIFSAN symposium, and the scientific and technical information shared at the symposium was considered in the development of this White Paper.

3. IWGACP Action Plan and Public Meeting

The IWGACP was asked to engage in the development of standardized testing methods for asbestos and other mineral particles of concern that could potentially affect cosmetic product safety. A first step in this effort was to develop a full understanding of why there is a lack of consistency among asbestos-testing methodologies focusing on mineral particle terminology, differences in analytical methods and characterization, and differing criteria for counting and laboratory reporting of test results. Thus, IWGACP evaluated current asbestos-testing methods seeking to understand whether definitions of terms and criteria related to characterization of asbestos minerals are applicable to the analysis for asbestos in talc-containing cosmetic products (See ***Appendix F.5***).

[5] https://jifsan.umd.edu/.
[6] https://jifsan.umd.edu/events/2018-asbestos-in-talc-symposium.

Some of the issues that remained unanswered following the JIFSAN Symposium included: appropriate terminology for the mineral particles identified by electron microscopy, characteristics to define a reportable particle, optimal analytical techniques, and information to be presented in reports from analytical laboratories. These issues formed the starting point for IWGACP's deliberations.

IWGACP members reviewed a large body of scientific information, dating from the 1970s to the present, pertaining to the current understanding of the relationship between health effects and physical-chemical attributes of respirable silicate mineral particles found in talc. The collective experience of IWGACP SMEs was leveraged to explore potential changes to current approaches for monitoring asbestos and other mineral particles in talc and talc-containing cosmetic products. For efficiency, three subgroups, all of which contributed to the scientific opinions presented in this White Paper, were established to address the following major topic areas: (1) terminology and definitions of asbestos and other mineral particles of health concern in talc; (2) development of a robust analytical protocol for detecting asbestos and other mineral particles of health concern in talc and consumer products containing talc; and (3) data reporting and analysis.

Faced with the question of how to identify minerals of concern in talc detected by microscopy, the IWGACP attempted to focus on terms that were relevant to the testing of talc intended for use in cosmetics and cosmetic products containing talc. Thus, IWGACP developed a glossary of key terms used in this White Paper which is provided in the ***Section XVI***.

Public Meeting and Docket. On February 4, 2020, the FDA held a public meeting that had more than 500 attendees, and opened a public docket[7] in order to discuss and obtain scientific data and information on topics related to asbestos-testing of cosmetic products with talc as an ingredient, testing methodologies, terminology, and criteria that could be applied to characterize and measure asbestos and other potentially harmful elongate mineral particles (EMPs) that may be present as contaminants in such products. At that meeting, IWGACP members presented preliminary recommendations on testing methods, including criteria to be used for asbestos fiber identification and counting. The IWGACP considered the public comments in drafting this white paper. The Executive Summary and related presentations at the public meeting were meant solely to solicit scientific feedback on the issues raised and were not intended for any other purpose. In addition to 23 public comment presentations at the public meeting, 46 comments were submitted to the docket, which were evaluated by the IWGACP and incorporated into this White Paper, as appropriate, in the development of these scientific opinions.

[7] https://www.regulations.gov/docket/FDA-2020-N-0025.

APPENDIX B: ANALYTICAL METHODOLOGY

1. Summary of Analytical Approach

The IWGACP advises that a combination of polarized light microscopy (PLM) and transmission electron microscopy (TEM), with optional X-ray diffraction (XRD) and scanning electron microscopy (SEM), should be used to achieve the sensitivity to detect and identify talc, asbestos, and other mineral particles at ≥0.5 µm length with AR ≥3:1 (**Figure B-1**).

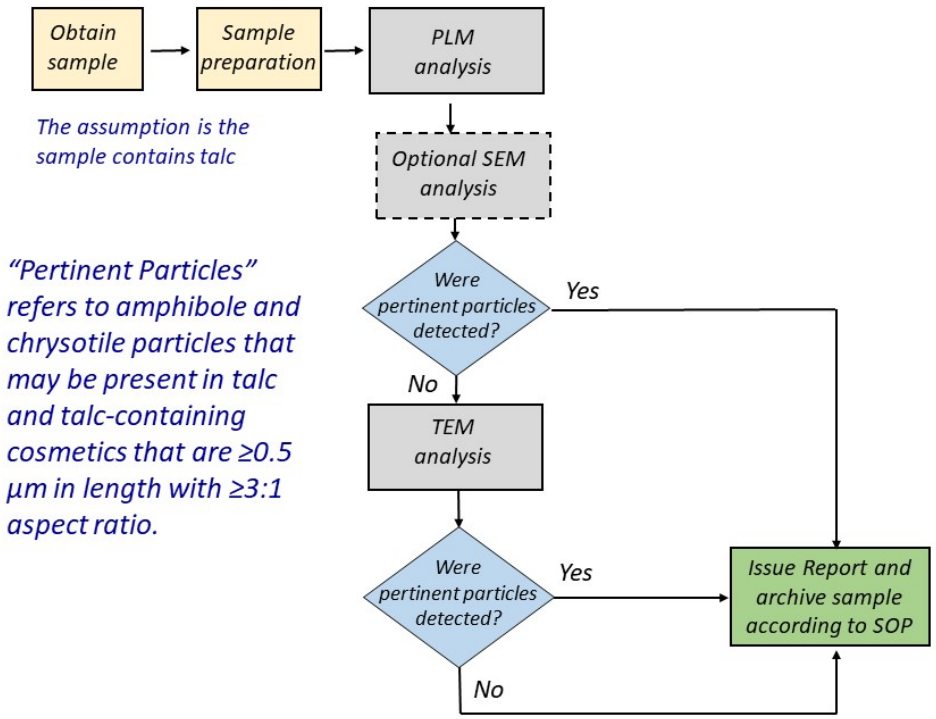

Figure B-1. Integrated approach to analysis of talc and talc-containing cosmetics for the presence of asbestos and other mineral particles. "Pertinent particles" are defined as any amphibole and chrysotile particle with a length ≥0.5 µm and a minimum AR of 3:1. The **SAMPLE** would include talc or talc-containing cosmetic products. **Sample Preparation** is any preparation (e.g., mixing for homogeneity, removal of moisture, removal of organic material, concentration of mineral particles from the sample) of a representative sample. This process may be different for talc or talc-containing cosmetics. **PLM** is used to visualize and characterize small minerals in products and can be used to discriminate minerals based on crystal structure using index of refraction liquids. If amphiboles or chrysotile are present in the sample using PLM, the analyst should conclude the sample contains these particles ("Yes") and report the observation (record data). No further analysis may be required. If PLM results are negative ("No"), electron microscopy *should be* performed. The sample may be analyzed by **SEM** (optional), but *should be* analyzed by **TEM** to achieve the analysis requirements to measure and identify amphiboles and chrysotile at ≥0.5 µm length with AR ≥3:1. The analyst is expected to report the quantification and mineral identification of amphiboles, chrysotile and other mineral particles meeting the criteria of ≥0.5 µm length with AR ≥ 3:1.

2. Elemental Analysis

There are two levels at which elemental analysis could occur: (a) analysis of all elements within the initial talc sample (as received or during sample preparation); and (b) elemental determination within individual particles during electron microscopic analysis. The IWGACP advises that the latter [elemental analysis of individual particles using TEM with energy dispersive X-Ray spectroscopy (EDS)] should be conducted on all suspect asbestos and amphibole particles. The analysis of all elements within a bulk sample is not commonly practiced at this time but could be conducted in the future to help identify talc provenance.

3. Light Microscopy

PLM is a visible light microscopy method that has been used to analyze many types of materials for the presence of asbestos. Identification of the six types of asbestos by PLM is based on optical properties of structures meeting dimensional criteria specified by the method. PLM uses polarized visible light to analyze samples immersed in liquids with precise refractive indices and is a valuable tool in the detection and identification of asbestiform mineral particles. PLM is a required method in many asbestos testing regulations and is also in guideline methods issued by federal agencies and international organizations. For this reason, the IWGACP supports PLM as a necessary analytical method for the analysis of amphibole, chrysotile, and other minerals of concern in talc, and has included it in the analytical approach outlined in **Figure B-1**.

Specific guidelines exist for the preparation and analysis of samples by PLM, including the use of refractive index liquids to determine the mineral nature of the particles (e.g., NIOSH Method 9002). The NIOSH method and other documents provide recommendations and guidelines for specific components of PLM analysis including: essential equipment requirements and performance; mineralogical and performance standards; sample preparation; standard operating procedures (best practices); statistics (how many particles, mass, or fields of view should be analyzed) [Crane, 1995 (OSHA 1901.1001); CTFA J 4-1; EPA 1993 (EPA/600/R-93/116); McCrone, 1974; NIOSH Method 9002; OSHA ID-160 (1997)].

Phase contrast microscopy (PCM) is another light-based method used to detect asbestos particles, which is typically used for air samples collected on filters (EPA-600/4-85-049; NIOSH 7400) and cannot be used for bulk materials like talc. The utility of PCM, like PLM, for analysis of amphibole, chrysotile, and other mineral particles $\geq$0.5 µm, AR $\geq$3:1, is affected by the limitations of resolution when using visible light. Light-based analytical methods other than PCM have been used to detect and analyze asbestos and other amphibole mineral particles. They have not been adopted by regulatory agencies for the detection, analysis, and quantification of asbestos, so their utility is questionable; however, they should be mentioned because research has been conducted on these various methods for detecting asbestos. These methods include stereomicroscopy [EPA, 1993 (EPA/600/R-93/116); Australian Standard AS 4964-2004],

darkfield microscopy (James et al. 1987), and Raman spectroscopy (Bard et al. 1988; Rinaudo et al. 2005).

There is a limit to the resolution of visible light microscopes. Because the shortest wavelength of illuminating visible light is approximately 0.4 µm (400 nm), according to Abbe's equation [8], the limit of resolution would be 0.2 µm. Thus, for a particle that is 0.5 µm in length, the width of 0.17 µm (3:1 AR) would be below the limit of resolution of visible light. Because of these fundamental physics of light, many publications have indicated that the limit of resolution of PLM is ≥0.2 µm [0.20 µm (OSHA ID-160); 0.25 µm (EPA 600/R-93/116); 0.3 µm (NIOSH method 9002); 0.4 µm (Crane, 1995. NIOSH ID-191)]. The limitations of light microscopes as compared to electron microscopes are evident when attempting to analyze mineral particles <5 µm and ≥0.5 µm, AR ≥3:1 in any products that contain talc.

In summary, the IWGACP regards PLM as having substantial limitations in its ability to detect, resolve, and identify individual fibers of asbestos and other amphibole minerals that are ≤5 µm in length with AR ≥3:1. Therefore, even if asbestos and other amphibole mineral particles are not detected using PLM, the IWGACP advises that electron microscopy (e.g., TEM) should be used to analyze talc and talc-containing cosmetics for asbestos and other amphibole mineral particles having length ≥0.5 µm and AR ≥3:1.

4. TEM

TEM is a high-magnification microscopy technique in which a beam of electrons is transmitted through a specimen to form an image with much higher resolution than that achievable using visible light. The IWGACP advises that all analyses for asbestos and other amphibole mineral particles of interest in talc and talc-containing cosmetics should include TEM analysis (unless sample is rejected due to prior detection of asbestos with XRD or PLM). Whereas the limit of resolution of PLM (≥0.2 µm) is limited by the wavelength of visible light, the limit of resolution of TEM would be limited by the wavelength of the incident electrons (<0.0037 nm at 100 kV). The limit of resolution of a 100-200 kV TEM is generally considered to be approximately 0.1-0.2 nm (0.0001-0.0002 µm) owing to imperfections in electron microscope equipment. [9] In keeping with the superior detection limits of TEM, which has a resolution approximately 1000-times greater than that of PLM, the IWGACP advises that talc-containing cosmetics should be analyzed using TEM for the presence of asbestos and other amphibole mineral particles ≥0.5 µm in length with AR≥3:1.

[8] The limit of resolution (minimum separation of two objects) for all microscopes is defined with Abbe's equation, d= (0.612 λ)/*n* sin *a*, where *d* = resolution, λ = wavelength of imaging radiation, *n* = index of refraction of medium between point source and lens relative to free space, and *a* = half the angle of the cone of light from specimen plane accepted by the objective (half aperture angle in radians). *n* sin *a* is sometimes referred to as the numerical aperture.

[9] https://advanced-microscopy.utah.edu/education/electron-micro/

In TEM analysis, electron diffraction patterns are created when electrons pass through atoms of a particle. When electrons pass through crystals, the atomic repeat patterns create unique diffraction patterns that are diagnostic of the crystal structure and thus contribute to the unequivocal identification of the mineral particle. This creation of diffraction patterns is used in electron microscopy to determine the crystal structure along the length of particles (selected area electron diffraction (SAED)); analysis from the perspective of at least two zone axes in the particle can reduce ambiguity in mineral identification. This capability of TEM to conduct SAED is invaluable for identification of chrysotile and amphibole minerals in talc samples.

EDS is used to conduct qualitative and semi-quantitative elemental analyses (from boron to uranium excluding the noble gases) of a particle under the electron beam. The beam electrons interact with element electrons resulting in the ejection of electrons from the atoms of the irradiated particle, creating a cascade of subatomic shell changes and the ejection of X-rays which are characteristic for each element (quantized). The resulting spectrum shows the energies and corresponding intensities of X-rays that correspond to atomic transitions characteristic of the irradiated elements. The elemental composition obtained by EDS can be used in conjunction with information about the crystal structure obtained by SAED to determine the mineral identity of each particle and is considered an essential method for mineral identification. EDS should be calibrated according to the TEM instrument manufacturer and have resolution compatible with current industry standards (131-133 eV resolution to discriminate K and L lines from elements). The most pressing consideration is that the EDS unit is calibrated within the range of atoms expected to be present in talc considering other minerals that may be present in talc (i.e., Mg, Si, Na, Ca, Fe, O, Mn, Al) (Goldstein et al., 2017; Newbury and Ritchie, 2016).

The IWGACP advises that all analyses for asbestos and other amphibole mineral particles of interest in talc and talc-containing cosmetics should include TEM analysis, unless the sample has been rejected due to prior detection of asbestos with XRD or PLM. TEM is not a substitute for PLM, but rather, a complementary technique. Whereas TEM offers the advantage of resolving short and thin particles, only a relatively small amount of sample can be analyzed. PLM, by contrast, offers the advantage of inspecting a larger sample size, albeit at much reduced resolution. A finding of fiber bundles by PLM indicates that if sufficient sample is examined, individual fibers will be found by TEM also; however, as we have seen with a great many samples, a negative finding by PLM cannot predict a negative finding by TEM.

The TEM analyses should be conducted by a microscopist trained and experienced in TEM imaging of minerals (see ***Appendix H***). The electron microscope must produce accelerated electrons with enough energy to penetrate the particle object and produce diffracted electrons. The instrument should be capable of accelerating electrons with 100-120 kV for penetration of all possible EMP particles. The accumulation of X-rays for EDS should be sufficient for elemental identification and rapid enough to avoid loss of cations (e.g., Na^+) and change or loss of structure.

TEM analysis for presence of chrysotile and amphibole in talc and talc-containing cosmetics should follow guidelines in existing protocols regarding the number of locations on the mineral particle to obtain EDS spectra and SAED diffraction patterns [40 CFR § 763 Subpart E, AHERA; NIST NVLAP Handbook 150-13:2006; NIST HB 150-13 Checklist; ISO 10312:2019; EPA, 1994 (EPA/600/R-94/134 100.2); NIOSH 7402; NBS Publ. 619; EPA 2014]. The choice of electron source, accelerating voltage, beam alignment, and quality, sample stage holder, grid, sample coating, detector, and the methods of calibration and QA/QC should all be based on reference to minimum requirements for laboratories accredited to test for asbestos.

There are currently no NIST standard materials (SM) or standard reference materials (SRMs) for talc containing <1% asbestos and amphibole particles. As in the case for asbestos analyses performed on air samples and bulk materials, when analyzing talc or talc-containing cosmetic samples, suitable reference materials should be developed. These reference materials are critical for classification and resolution of ambiguities in mineral identification, for EDS and SAED performance checks, and for understanding method efficiency.

5. SEM

In SEM, a beam of accelerated electrons interacts with the surface of the particle, and the scattered electrons can be used to create an image of the object. As with TEM the accelerated electrons can eject an electron out of atomic orbitals (e.g., K, L, M), resulting in X-ray emissions that are characteristic for the element and orbitals (EDS spectra).

Compared with TEM, SEM has the advantages of scanning large areas of sample at low to high magnification, providing surface and three-dimensional imaging. Similar to TEM, SEM can be used to obtain semi-quantitative elemental analysis using EDS, and also supports electron-microprobe analysis for elemental analysis. One current disadvantage is that SEM does not support SAED analysis for crystal structure determination, though there has been some recent research into determination of crystal structure using electron backscatter diffraction (EBSD) with SEM for identification of asbestos. For these reasons, IWGACP believes that SEM may be used as an adjunct to TEM; however, at the present time it cannot substitute for TEM.

Scanning electron microscopes can be equipped with multiple detectors that are useful in imaging and analysis of the particle under observation. Secondary electron detectors, including the Everhart-Thornley style of detector, produce an image based primarily upon the topography of the particle. Backscattered electron detectors produce an SEM image based on the atomic density of the particle under the electron beam, wherein, the higher the atomic number of the atom the “brighter” the object appears in the resultant image. Certain EBSD cameras have recently been used to identify the crystal structure of materials in the electron beam (Bandli and Gunter, 2014) and may overcome the inability of SEM to aid in determining crystal structure.

The SEM instruments should be calibrated with metric standards, such as NIST RM 8820, or commercial standards that are NIST-traceable, such as the MRS-3, 4 or 6 (Geller MicroÅnalytical Laboratory).

The SEM should have an EDS detector to determine the elemental composition of mineral particles in the electron beam. The considerations are the same as those for TEM/EDS (see above; also, Goldstein et al. 2017, and Newbury and Ritchie, 2016).

There are many NIST standards of defined elemental composition, commercial standards, and available substances (e.g., copper, nickel, gold, or silver wire) that could be used for SEM/EDS calibration and calibration checks. As with TEM, the most pressing consideration is that the SEM/EDS unit is calibrated within the range of atoms expected to be present in talc and asbestos and amphibole minerals that could be present in talc (i.e., Mg, Si, Na, Ca, Fe, O, Mn, Al).

Publications on the best practices of SEM analysis and guidelines for conducting SEM analysis of asbestos in samples should be consulted for any analyses (Goldstein et al. 2017; Newbury and Ritchie, 2016; ISO 14966:2002; Perry, 2004; National Bureau of Standards (NBS), Special Publication 619).

6. XRD

XRD is used to generate diffraction patterns following X-ray irradiation, and the patterns can be compared to published diffraction patterns for mineral identification. XRD samples must be powdered as much as possible for optimum detection of minerals (45 μm for qualitative analysis; 10 μm for quantitative analysis; EPA, 1993). In published methods for cosmetic (CTFA J4-1) and pharmaceutical (USP) grade talc, XRD is a screening method for determining the presence of amphibole or serpentine asbestos. XRD has a nominal sensitivity of 0.5% by weight for detection of amphibole in talc (Block et al. 2014; CTFA J 4-1) and is of limited use to screen for serpentine due to interference when chlorite, a common accessory mineral in talc ores, is present. Thus, XRD may have limited utility to screen for amphibole and serpentine in many of the cosmetic products that contain talc. IWGACP agrees with USP's talc expert panel regarding the shortcomings in sensitivity and specificity of XRD and their recommendation for use of PLM if XRD is negative for amphibole and serpentine (Block et al. 2014). The IWGACP advises that analysis by TEM in addition to PLM, should be used regardless of the XRD result with talc-containing cosmetics.

XRD analysis can be conducted using one of a range of X-ray tubes including copper, cobalt, or molybdenum, as needed. The XRD goniometer should be configured for theta (θ):2θ or θ:θ rotations. The data analysis should compare the results with those included in standard databases, such as the International Center for Diffraction Data (ICDD) powder diffraction file.

Best practice and guidelines for XRD operation are available (Buhrke et al., 1999; Bish and Post, 1989; Jenkins and Snyder, 1996; EPA, 1993 (EPA/600/R-93/116); Tomaino, 1994; U. S. Geological Survey Open-File Report 01-041; NIOSH 7500; NIOSH 9000; CTFA J 4-1; USP General Chapter <941>; ISO 22262-3:2016). Equipment performance is determined by quality control (QC) measurements that can be obtained with analysis of standard reference materials (SRMs), such as silicon (NIST SRM 640d), a corundum plate (NIST SRM 1976), or NIST powder diffraction SRMs.

7. Reporting of Relevant Attributes

Generally, the testing of talc and talc-containing cosmetic products involves multiple, complementary methods of analysis that may corroborate the findings regarding minerals present in the samples. **Table B-1** summarizes the attributes and measurements of each of the analytical methods that the IWGACP considers relevant for the testing of a sample of talc intended for use in cosmetics or talc-containing cosmetic products.

Table B-1 Summary of Useful Analytical Techniques and Corresponding Attributes and Measurements to Analyze Talc and/or Talc-containing Cosmetics

Technique	Attribute to Report	Measurement and Utility
PLM	Particle mineral type including any applicable inference to growth habit based on morphology (e.g., tremolite asbestos, chrysotile, asbestiform winchite-richterite)	Representative images useful to identify (with greater specificity than XRD) mineral type (based on particle optical characteristics) and morphology; may be used to quantify or estimate amount of each mineral type (see "point counting" methods); particle morphology (i.e., "bundles of sticks" [10]) may be indicative of "asbestiform" habit; regarded to have limited or no utility for detection of chrysotile in talc or talc-containing cosmetics
TEM	Particle morphology	Representative images showing morphology (in conjunction with SAED can be diagnostic for chrysotile) accompanied by tabulations showing each mineral particle's length and width (and calculated aspect ratio) [11]
TEM/EDS	Elemental composition of particles	Representative spectra and tabulations indicating which elements (e.g., Ca, Mg, Si, Fe, O, etc.) are present; semi-quantitative analysis of elemental composition is used in conjunction with TEM/SAED to help identify mineral type

[10] See CTFA J-4-1 for description of morphology of amphibole asbestos.
[11] Numerical values of particles counted, and number of amphiboles and chrysotile detected should be reported.

Technique	Attribute to Report	Measurement and Utility
TEM/SAED	Crystal structure of particles	Representative electron diffraction patterns are generated showing spacing of atoms; quantitation of distances between atoms and adjacent planes of atoms in crystal is used in conjunction with TEM/EDS to help identify mineral type; at least two zone axis measurements (from different angles) may be necessary to identify certain minerals
SEM	Particle morphology	Representative images and tabulations of particle length, width (aspect ratio); may provide enhanced visual detail (to supplement TEM) useful to determine if a particle is "asbestiform"
SEM/EDS	Elemental Composition of particles	Representative spectra and tabulations indicating which elements (e.g., Calcium (Ca), Magnesium (Mg), Silicon (Si), Iron (Fe), Oxygen (O), etc.) are present; semi-quantitative analysis of elemental composition
XRD	Mineral (group) type (e.g., amphibole, serpentine, chlorite)	Identity and estimate of amounts of mineral types in a bulk sample (e.g., talc); generally not sensitive when asbestos is below 0.5%; appears most useful as a qualitative method to determine presence/composition of minerals and reporting estimated amounts of each mineral using terms such as 'trace', 'minor' and 'major'

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APPENDIX C:
TALC: PROPERTIES, TERMINOLOGY, COMMERCIAL USE AND GEOLOGICAL CONSIDERATIONS

1. Chemical and Physical Properties of Talc and Applicable Terminology

Talc in its purest form is an especially soft, white, naturally occurring mineral of the sheet silicate group. The pure talc substance, i.e., $Mg_3Si_4O_{10}(OH)_2$, (**Figure C-1)** has a layered crystal structure consisting of repeating silicate units (sheets) surrounding a layer of brucite (MgO). These sandwich-like sheets are very weakly bonded, which allows sliding or shearing along these planes and accounts for the platy particle morphology and slippery feel of talc. Due to these properties, talc is the softest mineral known, having a hardness of 1 on the Mohs hardness scale of 1 to 10. Other physical properties relevant to talc's use in cosmetics include crystallinity, particle morphology (size and shape), and hydrophobicity (IARC, 2010).

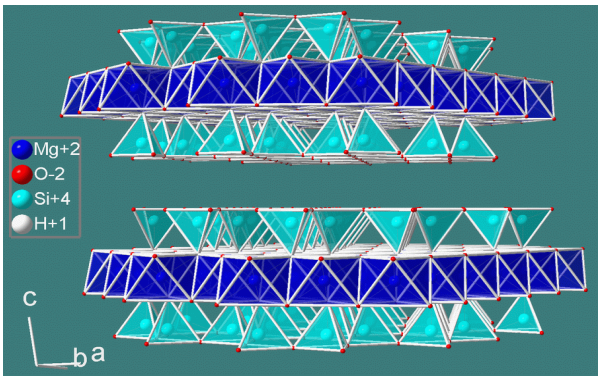

Figure C-1. **Structure of Talc.** The layered crystal structure of talc is responsible for its perfect cleavage and slippery nature. Source: IARC 2010.

Commercial talc ores have unique characteristic mineral compositions and impurity content due to regional variations in the conditions of their formation over geologic time (IARC, 2010; Piniazkiewicz et al. 1994; Zazenski et al. 1995; Van Gosen et al. 2004a; Buzon, 2016). In the crystal structure of talc, small amounts of aluminum, iron, manganese, titanium, nickel, and chromium may substitute for silicon and magnesium cations, while fluorine and chlorine anions commonly substitute for hydroxyl (OH) groups (Zazenski et al. 1995; Buzon, 2016). Some of these impurities, particularly iron, can impart a darker color to the talc, which is undesirable in cosmetics. Commercial talc ores may also contain or be in contact with other minerals, most commonly magnesium-rich carbonates, calcite, quartz, and chlorite. Certain talc ores may be associated with amphibole and serpentine minerals. The ores from which raw material talc powders are derived typically contain approximately 35% to 95% pure talc substance; thus, the

term "talc" has been used to refer to commercial minerals having as little as 35% content of the pure mineral.

The highest purity, whitest talc ores, consisting of predominately platy particles, are the preferred sources of raw material talc used to manufacture cosmetics (IARC, 2010; Jadhav et al. 2013; Fiume et al. 2015). The Personal Care Products Council (PCPC, formerly the Cosmetic, Toiletry, and Fragrance Association (CTFA)) in its quality standard (CTFA, 1976) defines ***Cosmetic Talc*** as follows: "cosmetic talc consists of a minimum content of 90% hydrous magnesium silicate, with the remainder consisting of naturally associated minerals such as calcite, chlorite, dolomite, kaolin, and magnesite; it contains no detectable fibrous, asbestos minerals." The definitions of talc in the respective food [Food Chemicals Codex (FCC)], drug (USP), and cosmetic (PCPC) standards (**see *Appendix F***) highlight the importance of selecting suitable deposits after careful consideration of the ore-forming geology and the mineral composition of the ore.

Talc raw material powders are produced from the mined ore by a series of steps that generally include beneficiation by means of hand-sorting, flotation, tabling (gravity) and/or magnetic separation, and grinding. Talc raw materials for cosmetics may also be heat-treated to minimize microbial contamination. Talc ores are ground to achieve particle size distributions appropriate for use in the manufacturing of cosmetic products; for example, talc for use in body powders is often ground such that 95-99% will pass through a 200 mesh (74 µm) sieve, whereas talc for use in pressed powders is often ground more finely, such that 95-99% will pass through a 400 mesh sieve (37 µm) (Piniazkiewicz et al. 1994; Zazenski et al. 1995; Jadhav et al. 2013; Fiume et al. 2015).

The ***particle morphology*** (shape) of talc is a function of its crystal growth habit and how the ore was processed into powder and can generally be categorized as either platy or non-platy. Examples of both types are given in **Figure C-2**.

Platy Talc. Under an electron microscope, groups of adjacent particles have a foliated (lamellar) appearance (**Figure C-2(A)**). Consistent with their layered crystal structure, individual talc particles that are liberated by grinding or attrition are typically described as having a "platy" or plate-like appearance **(Figure C-2(B**)). An image of a curved particle of platy talc that could have conceivably formed during processing, e.g., when the ore was milled, is shown in **Figure C-2(C).**

Non-Platy Talc. Talc may also exhibit non-platy morphology. Certain non-platy particles of talc, including particles not identifiable as the discrete mineral talc, have collectively been referred to as "fibrous talc." Examples of these non-platy particles are provided in **Figures C-2(D-F).**

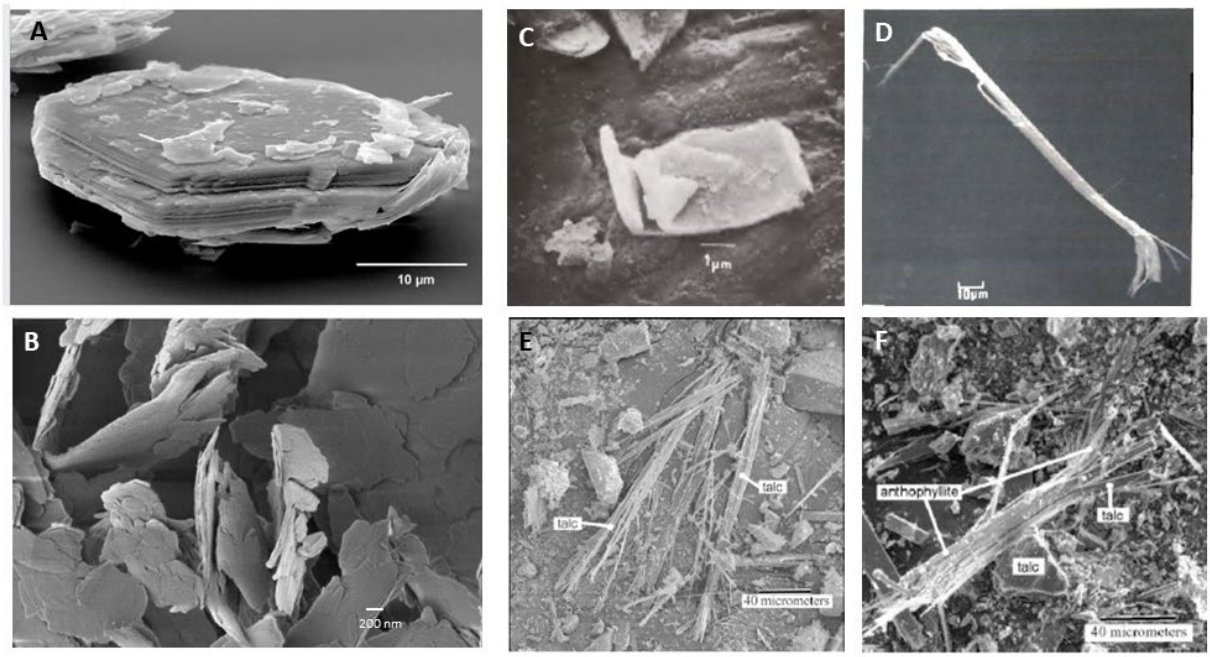

Figure C-2: Morphology of Talc. Scanning electron microscope (SEM) images. Cosmetic and pharmaceutical grade talc predominately consists of flat, "platy" particles such as shown in panels (A) and (B) and may occasionally contain curved platelets as shown in panel (C). In the case shown in panel (C) it is considered advantageous to view the particle from multiple angles to avoid incorrectly characterizing this particle as a type of non-platy talc. Although evidently less common in grades of talc used to manufacture cosmetics, talc particles having non-platy morphologies, examples of which are shown in panels (D), (E) and (F), have been observed in raw material talc powders. Panel (D) shows a 500x image of a talc particle of unknown provenance classified by the author as "non-asbestiform fibrous talc" at 500X. Panels (E) and (F) show talc fibers that formed via a transition in which talc replaced amphibole. In the fibrous particle in panel (F), the replacement of amphibole to talc has been incomplete, resulting in "transitional fibers" composed of both talc and amphibole. The specimens in panels (E) and (F) were from the Gouverneur mine in upstate New York. Photo credits: (A) from MVA Scientific Consultants https://mvascientificconsultants.com/sem-analysis-testing-services-lab/talc-particle-electron-microscope-image; permission received from Steven Compton on 9/24/20; (B) from Block et al. (2014) with permission from G. Tomaino on 12/8/20; (C) From Parmentier and Gill, 1977; (D) From Campbell et al. 1977; (E-F) from Van Gosen et al. 2004a.

Although the term "asbestiform" has also been used to describe the morphology of some talc particles described as "fibrous", "asbestiform talc" is not defined nor regulated as a type of asbestos in federal asbestos regulations. A type of particle having a fibrous morphology and composed of intergrown talc and amphibole in various proportions, has been referred to as "transitional" or ''intermediate" talc. These types of particles, depicted in **Figures C-2(E)** and **(F),** have been observed in the tremolite-anthophyllite-rich talc deposits of the Gouverneur mining district in New York (McNamee et al. 2015). Talc having fibrous character may be found in appreciable amounts in grades of talc used to manufacture industrial products, whereas talc ores with predominantly platy character are typically used for the manufacture of cosmetics (see below) (Zazenski et al. 1995; IARC, 2010).

2. Commercial Use of Talc

Talc is a raw material found in many products that consumers use daily. An estimated 640,000 tons of raw material talc was consumed by the US in 2019. Domestic talc production was mostly from Montana, Texas, and Vermont, with imports primarily from Pakistan, Canada, and China (Bolen (USGS), 2020). Net import reliance in 2019, as a percentage of apparent consumption (imports minus exports), was 11 percent. Data from annual reports by USGS since 1996 (USGS Open File Reports, Talc and Pyrophyllite), indicate that historically, cosmetics account for only a very small percentage of total commercial talc use. These reports also signal a trend toward increased reliance on imported talc.

Many talc-containing consumer products, including cosmetics, are also imported. For example, in 2016, approximately 29,000 companies from 181 countries (especially Canada, France, China, India, Mexico, Korea, and Taiwan) were manufacturers or exporters of cosmetics to the U.S. (Abram, 2017). Little or nothing is known about cosmetic talc sourcing or supply chains.

Talc raw materials can be classified into two general categories related to their end use: 1) talc grades labeled for use in manufacturing food, drugs and cosmetics and 2) talc grades for industrial use, i.e., talc intended for use in manufacturing products not regulated by the FDA. Raw material talc is used in a wide variety of FDA-regulated products where it can function as a color additive, a carrier, a thickener, a strengthener, an absorbent, an anti-sticking agent, an anti-caking agent, and a lubricant (Jadhav et al., 2013). In cosmetics, talc can be used to absorb moisture, prevent caking, contribute to the opacity of facial makeup, and confer a soft and slippery feel (Zazenski et al. 1995). Industrial-grade talc is used in plastics, ceramics, paint, paper, rubber, art materials, building materials, joint fillers, grouts, fire extinguishers, fertilizers, insecticides and herbicides (IARC, 2010; USGS open file reports and Bolen 2020). Since at least 1996, <10% of talc raw material usage has been in FDA-regulated products. Only about 2% of all talc sold in the US in 2019 was used in cosmetics (e.g., body powders and eye and face makeup). (USGS Open File Report, Talc and Pyrophyllite - 2020).

3. Geology of Formation of Talc Deposits and Accessory Minerals

As with all mineral ore deposits, the geologic environment determined the physical characteristics and mineral composition of each talc deposit. Thus, local and regional geologic processes, and mechanisms of formation classified as “hydrothermal” or “metamorphic” (see below), ultimately influenced if a talc deposit was of adequate size and mineral quality to be a source of raw material, and influenced the types and amounts of other minerals (accessory minerals). As shown in **Table C-1** commercially significant deposits range in purity. The accessory minerals in commercially significant talc deposits most often include magnesium-rich carbonates, calcite ($CaCO_3$), and minerals in the chlorite group; noteworthy with respect to

quality of cosmetic talc, accessory minerals may on occasion include quartz and minerals in the amphibole and serpentine groups, including the six which are defined as asbestos in federal regulations. (See ***Appendix D*** for more information on the types of asbestos and asbestiform minerals.)

Table C-1. Mineral composition (wt%) of talc from various locations. Purity and major and minor accessory mineral profiles of commercially significant talc deposits. Source: IARC Monograph 93 on Carbon Black, Titanium Dioxide, and Talc (2010).

Mineral	Montana	Vermont	North Carolina	New York[a]	California	France
Talc	90-95	80-92	80-92	35-60	85-90	70-90
Tremolite	-	-	-	30-55	0-12	-
Anthophyllite	-	-	0-5	3-10	-	-
Serpentine	-	-	-	2-5	-	-
Quartz	<1	<1	1-3	1-3	<1	<1
Chlorite	2-4	2-4	5-7	-	-	10-30
Dolomite	1-3	1-3	2-4	0-2	0-3	-
Calcite	-	-	-	1-2	-	-
Magnesite	0-5	0-5	-	1-3	-	-

From Harben & Kuzvart (1996)
[a] Gouveneur District

Metamorphism or hydrothermal processes led to the formation of important talc deposits. Metamorphism, in a geologic context, is a change in the composition or structure of a pre-existing rock by the introduction of heat, pressure, and/or deformation, and often, fluids. Two types, contact and regional metamorphism, caused the formation of certain commercially significant talc deposits. In each type of metamorphism, the rock that was replaced by talc is magnesium (Mg)-rich, usually either a serpentine-rich rock (serpentinite) or dolomite (a Mg-rich carbonate). In formation of talc deposits by contact metamorphism, magma intruded a Mg-rich rock, introducing heat and silica-rich fluids. In formation of talc deposits by regional metamorphism, compression of rocks across a region provided heat and pressure and moved silica-rich fluids into Mg-rich rock units (Block et al, 2014, Buzon 2016, Van Gosen et al 2014a). Alternatively, talc resulting from a hydrothermal processes (hydrothermal talc) forms when volatile fluids (water, CO_2, etc.) and solutions are heated by deeply buried magmatic bodies, rise and percolate through the overlying rocks, altering the composition of rock bodies to form a significant talc deposit. Some high-purity talc deposits of large size were formed by hydrothermal processes, in which fluids containing silica, heated by magmatic bodies at depth,

upwelled through fractures and reacted with magnesium carbonates (dolostone) in overlying strata (Block et al, 2014, Buzon 2016, Van Gosen et al 2014a).

A study by the USGS (Van Gosen et al. 2004a) showed, by collecting and analyzing samples from former talc mines, that the type of talc-forming process, and corresponding differences in the conditions of temperature and pressure, affected the potential for amphibole minerals to co-occur with the talc. It was thus found that talc deposits that formed via hydrothermal mechanisms, involving volatile fluids and lower temperature and pressure, consistently lack amphibole as accessory minerals. For example, samples taken from hydrothermal talc deposits occurring in southwest Montana consistently lacked amphiboles. Alternatively, samples from talc deposits that formed at higher temperature due to regional or contact metamorphism, consistently contained amphiboles intimately associated with the talc, including amphiboles which crystallized in the asbestiform habit. Samples representing the 45 mined and/or prospected talc-bearing deposits in the Death Valley region that formed by contact metamorphism consistently contained amphibole particles, mainly tremolite, in association with the talc. Many of the amphibole particles found in the talc in Death Valley display high aspect ratios and consist of bundles of fibers, i.e., show characteristics of the asbestiform habit (Van Gosen et al. 2004a, b).[12] **Figure C-3(A), (B)** and **(C)** are scanning electron micrographs of talc ores from the Death Valley region that were studied by the USGS. Images in **Figure C-3(D), (E)** and **(F)** show the appearance of amphibole particles found in talc-containing cosmetics that have undergone extensive processing from ore, i.e., through milling of the ore to produce cosmetic talc raw material and subsequent use of the raw material to manufacture cosmetic products.

Based on reports in the literature, anthophyllite asbestos, tremolite asbestos, actinolite asbestos, and chrysotile are the types of asbestos minerals most commonly associated with commercial talc deposits (Hopkins, 1914; Chidester, 1962; Neathery et al. 1967; Neathery, 1968; Van Gosen et al. 2004a, 2004b). In addition, asbestiform particles of the sodic amphibole minerals, winchite and richterite, have been identified in the talc ores of abandoned talc mines in Death Valley, California (Van Gosen et al. 2004a, b). Very recently, winchite and richterite were reported to be present in certain cosmetic products manufactured using talc as an ingredient.[13] Minerals in the serpentine group, such as antigorite, have also been reported in association with some talc deposits in the U.S. (Buzon, 2016). Moreover, in talc deposits that formed by the regional metamorphism of serpentinite, it is not unusual for cross-cutting veins

[12] Talc from this region was used for the manufacture of ceramic wall tiles and as an extender in paints (Van Gosen et al., 2004a, b). The Death Valley mines all ceased commercial operation by the 1980s at which point many of these properties had become part of the newly formed Death Valley National Park.

[13] Some third-party laboratories (not under contract to FDA) have reported findings of richterite and winchite in cosmetics to the FDA. These results have not been independently verified.

filled with chrysotile to occur in the serpentinite bodies that bound the talc zones (Chidester, 1962; Sanford, 1982).

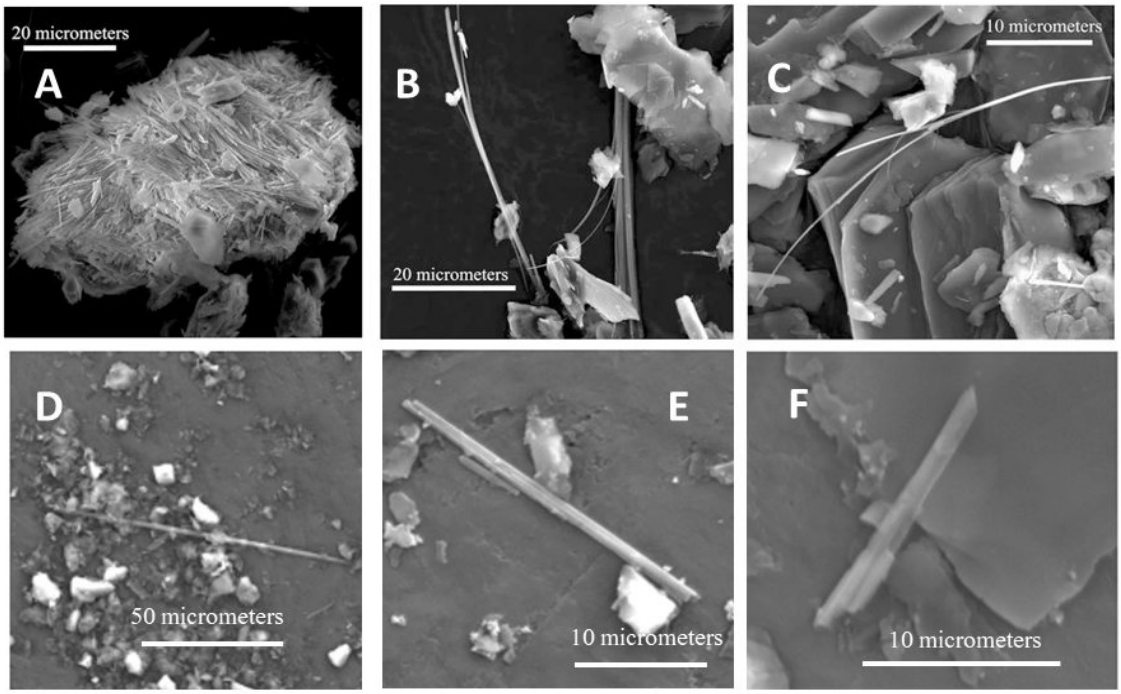

Figure C-3. SEM photomicrographs of minerals in talc ore (A-C) and talc-containing cosmetic products (D-F). (A) A bundle of fibrous tremolite mixed with talc platelets in talc-tremolite ore material (Warm Spring Canyon, Death Valley National Park, CA). **(B)** Asbestiform amphibole and platy talc in ore material (Grantham mine, Death Valley National Park, CA). **(C)** Coexisting platy talc with asbestiform amphibole (Acme mine, near Tecopa, CA). **(D-F)** Tremolite particles found in talc-containing cosmetic products. A-C: Photomicrographs from Van Gosen et. al. (2004a,b); D-F: Photomicrographs from OSHA (https://www.fda.gov/media/122413/download).

Commercially viable talc deposits that have geologies of formation and accessory minerals similar to the U.S. deposits occur in numerous countries, but with limited exceptions there is little published information about mineral composition profiles for talc ores located outside the U.S. (see e.g., Buzon, 2016; mindat.org, 2019). The rigor of scientific studies leading to talc mine selection and quality assurance/quality control (QA/QC) practices for routine monitoring of mineral composition are important considerations in the importation of talc ores, cosmetic talc raw materials and talc-containing cosmetic products.

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APPENDIX D: ASBESTOS: PROPERTIES, TERMINOLOGY, COMMERCIAL USE, PRESENCE IN TALC[14]

1. Nomenclature and General Chemical and Physical Properties of Asbestos

There are many definitions of **"asbestos"** used in the commercial, geological, and regulatory domains, partly because asbestos is not a single mineral, but rather six minerals having certain characteristics described below. As a commercial term, "asbestos" refers to a group of six minerals that have been mined and processed due to their commercially useful properties, including flexibility, durability, and heat-resistance. Mineralogists define "asbestos" more broadly, i.e., as those silicate minerals belonging to the serpentine and amphibole groups that have an unusual fibrous (asbestiform) crystal growth habit (as opposed to non-asbestiform or alternative habits of crystal growth) manifested by a particle morphology described below.[15] See Lowers and Meeker (2002) for more information regarding terminology and definitions.

Federal asbestos regulations and the test methods required to establish regulatory compliance with these regulations define asbestos using mineral and commercial nomenclature. Chrysotile, a member of the serpentine mineral group, accounts for greater than 95% of commercially used asbestos (VDH, 2019). In descending order of commercial significance, the other five types of asbestos, all of which are members of the amphibole mineral group, include: riebeckite asbestos (also known using the commercial term as crocidolite), grunerite-cummingtonite asbestos (also known using the commercial term as amosite), tremolite asbestos, anthophyllite asbestos, and actinolite asbestos. Although not currently recognized under the federal definitions of asbestos, some asbestiform amphibole-group minerals, notably asbestiform winchite and richterite, appear to have similar properties and health concerns.

Each of the six asbestos minerals has a chemically identical counterpart that crystallized in a non-fibrous form, or **habit.** The non-asbestiform minerals are readily distinguishable in appearance in bulk form. **"Asbestiform"** connotes a fibrous growth habit primarily in one dimension whereby the crystals form naturally as long, flexible fibers. Commercial asbestos consists of bundles of separable silicate **fibers** that when crushed or handled readily disaggregate and release microscopic fibers, or **fibrils**, that are **very thin (**typically ≤1 μm in width), **flexible**

[14] For more information on the history of asbestos as a commercial commodity and evolution of the regulatory framework for addressing commercial use of asbestos, see **Other Relevant Resources (Section D.4)**.
[15] Zoltai (1978) states the mineralogical and commercial definitions are "not coincident"; thus, asbestiform winchite-richterite, which could logically be defined mineralogically as a type of asbestos, is not included with the commercially designated asbestos minerals.

[high tensile strength (bend but not easily broken)] and **durable (**resistant to heat, chemicals, and electricity) and are the smallest indivisible unit of asbestos fibers.

Mineralogists distinguish fibrous minerals, which can be parted longitudinally using light pressure, from non-fibrous minerals, which do not separate into fibers and/or fibrils, but instead tend to fracture when subjected to force. Mineralogists use the term "**cleavage fragment**" to describe a particle derived from breakage of a crystal along planes of weakness. Amphibole cleavage fragments are derived from attrition of crystals that grew in the "**prismatic**" habit characteristic of the amphibole group of minerals (double chain silicates).

Whereas bulk forms of prismatic and asbestiform minerals can be readily differentiated, this distinction may be less apparent after a bulk amphibole mineral has been extensively processed. In addition to **"cleavage fragment,"** terms such as "**acicular**" ("needle-like") "**bladed**" (flat, not pointed) or "**splintery**" have also been used to describe amphibole particle morphology, implying the analyst has concluded the habit of growth to be non-asbestiform.

Figure D-1 provides images showing bulk morphologies of each of the six asbestos minerals defined as asbestos in federal regulations, alongside corresponding non-asbestiform minerals having the same chemical composition. [Note: The image of serpentine in **Figure D-1** does not specify the mineral type.] **Figure D-1** also provides general chemical formulas, shows locations of commercially significant asbestos deposits, and indicates chrysotile comprises the majority of commercially used of asbestos.

Table D-1 provides additional physical-chemical characteristics of the six regulated commercial asbestos minerals that may be useful to laboratories preparing and analyzing samples of talc and talc-containing cosmetics for asbestos.

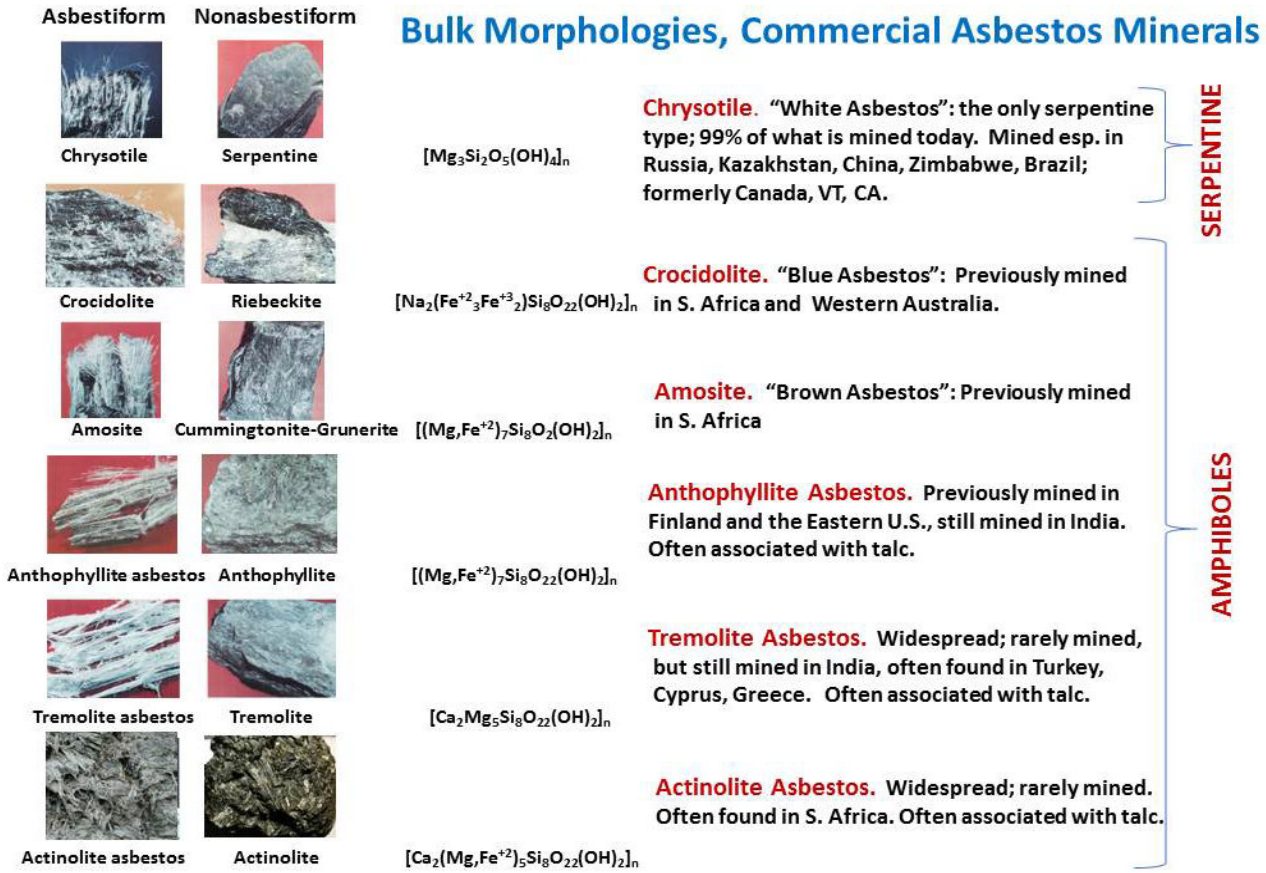


Figure D-1. Morphology of "Asbestos" Minerals, in Bulk Form before Processing. Source: Campbell et al. 1977 except for the two images of actinolite provided by Brad Van Gosen (USGS).

Table D-1. Nomenclature and Selected Physical and Chemical Properties of Commercial Asbestos Minerals. Common names, CAS numbers, synonyms, non-asbestos mineral analogues, idealized chemical formulae, selected physical and chemical properties of asbestos minerals

Group	Common Name	Cas No.	Synonyms	Non-Asbestos Mineral Analogues	Idealized Chemical Formula	Colour	Decomposition Temperature (ºC)	Other Properties
	Asbestos	1332-21-4*	Unspecified		Unspecified			
Serpentine group of minerals	Chrysotile	12001-29-5*	Serpentine asbestos; white asbestos	Lizardite, antigorite	$[Mg_3Si_2O_5(OH)_4]_n$	White, grey, green, yellowish	600-850	Curled sheet silicate, hollow central core; fibre bundle lengths = several mm to more than 10 cm; fibres more flexible than amphiboles; net positive surface charge; forms a stabile suspension in water; fibres degrade in dilute acids

Group	Common Name	Cas No.	Synonyms	Non-Asbestos Mineral Analogues	Idealized Chemical Formula	Colour	Decomposition Temperature (ºC)	Other Properties
Amphibole group of minerals	Crocidolite	12001-28-4*	Blue asbestos	Riebeckite	$[NaFe^{2+}_3 Fe^{3+}_2 Si_8 O_{22} (OH)_2]$	Lavender blue green	400-900	Double chain silicate; shorter, thinner fibres than other amphiboles, but not as thin as chrysotile; fibre flexibility: fair to good; spinnability: fair; resistance to acids: good; less heat resistance than other asbestos fibres; usually contains organic impurities, including low levels of PAHs; negative surface charge in water
Amphibole group of minerals	Amosite	12172-73-5*	Brown asbestos	Grunerite	$[(Mg,Fe^{2+})_7Si_8O_{22} (OH)_2]_n$	Brown, grey, greenish	600-900	Double chain silicate; long, straight, coarse fibres; fibre flexibility: somewhat; resistance to acids: somewhat; occurs with more iron than magnesium; negative surface charge in water
Amphibole group of minerals	Antho-phyllite	77536-66-4*	Ferroantho-phyllite; asbolen asbestos	Antho-phyllite	$[(Mg, Fe^{2+})_7Si_8O_{22} (OH_2]_n$	Grey, white, brown-grey, green	NR	Double chain silicate; short, very brittle fibres; resistance to acids: very; relatively rare; occasionally occurs as contaminant in talc deposits; negative surface charge in water
Amphibole group of minerals	Actinolite	77536-67-5*	Unspecified	Actinolite	$[Ca_2(Mg, Fe^{2+})_5Si_8O_{22} (OH)_2]_n$	Green	NR	Double chain silicate; brittle fibres; resistance to acids: none; occurs in asbestiform and non-asbestiform habit; iron-substituted derivative of tremolite; common contaminant in amosite deposits; negative surface charge in water
Amphibole group of minerals	Tremolite	77536-68-6*	Silicic acid; calcium magnesium salt (8:4)	Tremolite	$[Ca_2Mg_5Si_8O_{22} (OH)_2]_n$	White to pale green	950-1040	Double chain silicate; brittle fires; acid resistant; occurs in asbestiform and non-asbestiform habit; common contaminant in chrysotile and talc deposits; negative surface charge in water

*identified as asbestos by CAS Registry
NR, not reported
Source: Adapted from IARC Monograph 100C, p. 220. (IARC 2012).

2. Morphology of Asbestos and Amphibole Minerals

Morphology of asbestos traces to a specific habit of crystal growth germane to the amphibole and serpentine mineral groups, although characteristic asbestos structures - bundles of asbestos fibers - can be altered by subsequent processing. The term asbestiform, referring to morphology of asbestos, connotes this unusual habit of crystal growth and the resultant bundles of elongate mineral particles orient parallel to one another. When force is applied, these bundles can release smaller particles (i.e., asbestos fibers) that typically are <1 μm in width.

The lone asbestos type in the serpentine (sheet silicate) mineral group is chrysotile. The fibrous appearance (morphology) of chrysotile manifests due to a habit of growth in which the silicate sheets curved and formed hollow fibers during crystallization (Yada, 1967). Fibrils of chrysotile may be on the order of <10 nm in width.

Amphibole minerals crystallize in chains of silicate tetrahedra that are four tetrahedra wide and of great length (Zussman (1978)). The asbestiform habit arises from this fiber growth pattern predominately in one direction in the crystal**.** However, non-asbestiform varieties of amphibole minerals – including those that mineralogists would consider fibrous - can also result from this pattern of crystal growth. As shown in **Figure D-2** the most common habit in amphiboles is prismatic. Under most conditions, amphiboles form elongate crystals, due to their preferential growth along the "c axis". The asbestiform varieties of the amphibole minerals form fibrils (and fibers), with extremely thin dimensions along the "a" and "b" axes (generally <1 μm each) and a greater length along the "c" axis (typically at least 3 μm or more).

As depicted in **Figure D-2,** force applied to prismatic amphibole crystals can result in perfect cleavage along planes of weakness, often referred to as cleavage fragments. Similarly, attrition of bundles of asbestiform amphibole fibers can lead to structures such as the fibrils.

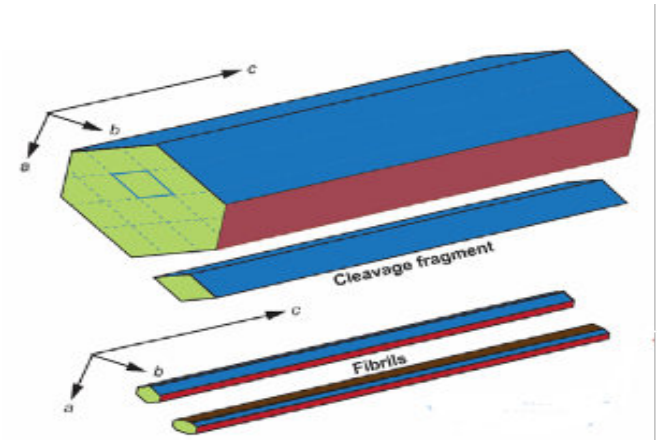


Figure D-2. Schematic of prismatic crystal showing preferential direction of growth in amphibole along the c-axis, i.e., oriented in the axis which contains the silicate chains. A cleavage fragment that can result from breakage along a plane of weakness in a prismatic crystal as well as asbestos fibrils that might result from attrition of a bundle of an

asbestiform amphibole are also shown. (Source: comment to FDA Docket #2020-N-2025, comment 46 by Laura M. Webb, Univ. Vermont) See https://www.regulations.gov/docket/FDA-2020-N-0025.

Alternatively, fracture at points of structural weakness caused by defects in amphibole crystals can result in particles having random shapes. Consequently, significant variation in morphology of amphibole particles can occur even within a mineral deposit and it may be difficult to classify individual particles as being asbestiform or non-asbestiform.

The following (**Figures D-3(A-D)**) series of micrographs obtained using SEM show fiber "bundles" of the four most common asbestos minerals found in talc deposits, and asbestiform winchite-richterite (not currently regulated, but also known to occur in some talc deposits). However, as noted previously, bundles are perhaps less typically observed in milled talc powders due to attrition resulting in an asbestos particle population which may be dominated by individual fibers. Similar observations, indicative of attrition, have been made in other processed minerals that can contain asbestos, such as vermiculite.

Figure D-3 (A) Microscopic morphologies, types of asbestiform minerals potentially found in talc. SEM image of chrysotile and amphibole asbestiform minerals which may sometimes appear in talc. All photo from B. Van Gosen except: Winchite-richterite photo of sample from a location in Libby, MT. (Image downloaded from: USGS Microbeam lab website https://www.usgs.gov/media/galleries/fibrous-and-asbestiform-minerals) Chrysotile photo from presentation on "The Mineral Fibers of Potential Concern in Talc" by B.S. Van Gosen at JIFSAN "Asbestos in Talc Symposium" Nov. 28, 2018, https://jifsan.umd.edu/files/wordpress/wp-content/uploads/2018/12/Talc_Van-Gosen.pdf).

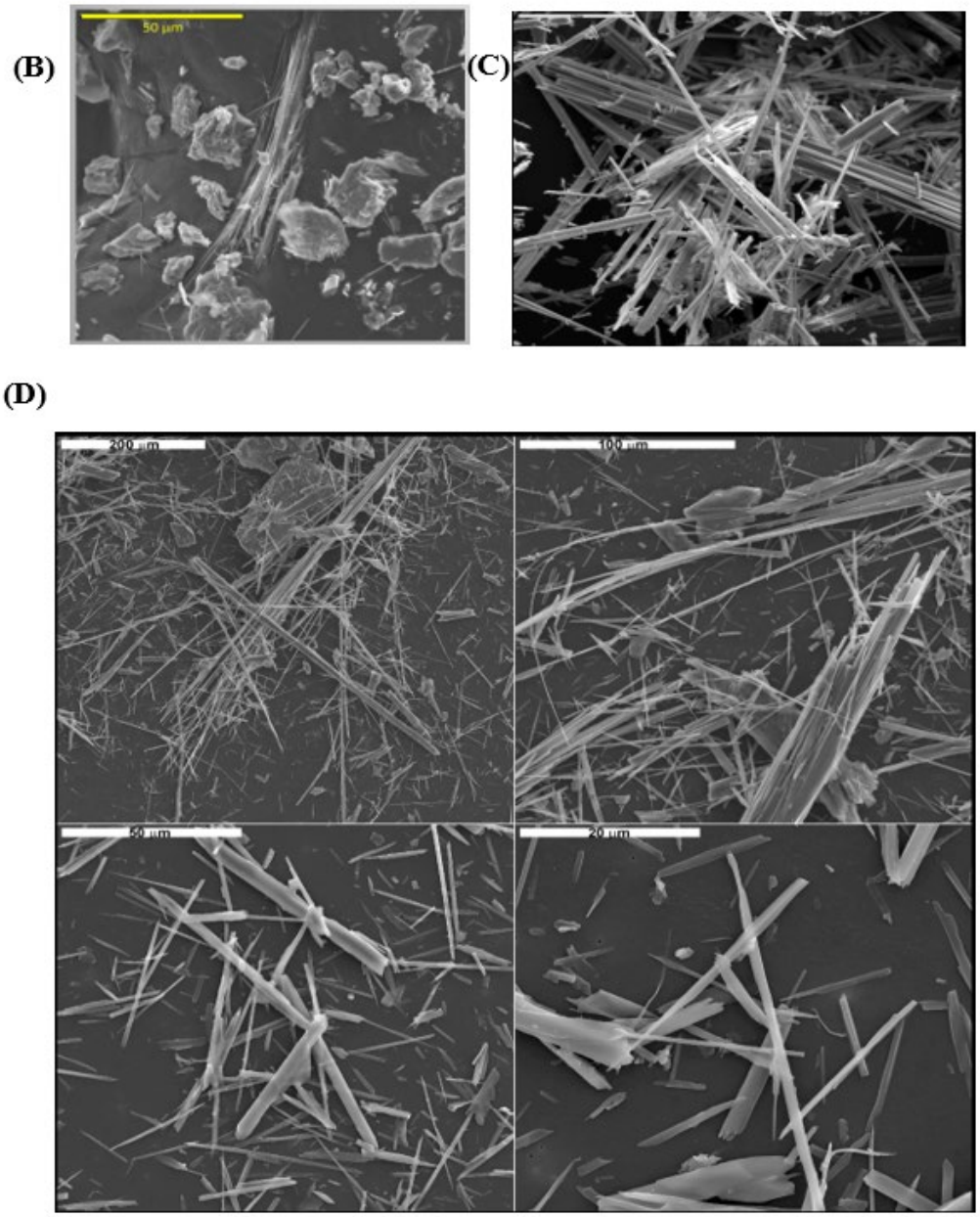


Figure D-3 (B). SEM image of tremolite asbestos fibers intermixed with platy talc. Sample was obtained from a location in Death Valley, CA. (Image downloaded from: USGS Microbeam lab website, https://www.usgs.gov/media/images/tremolite-asbestos). **(C). SEM image of anthophyllite asbestos fibers.** Sample was obtained from a location in GA. (Image downloaded from: USGS Microbeam lab website, https://www.usgs.gov/media/galleries/fibrous-and-asbestiform-minerals). **(D). SEM images of actinolite asbestos fibers.** The actinolite, collected by National Institute of Standards and Technology (NIST) at a construction site in Fairfax County, VA, was prepared and packaged by Research Triangle Institute, Research Triangle Park, NC and became known as NIST actinolite asbestos standard reference material® (SRM) 1867a. (Image downloaded from: USGS Microbeam lab website https://www.usgs.gov/media/images/nist-reference-material-1867a).

Because fiber bundles undergo attrition, it is difficult to draw conclusions about the (asbestiform/non-asbestiform) habit of any individual amphibole particle at the levels of magnification afforded by electron microscope. Electron microscope images that depict the range of mineral particle shapes that can be found in amphibole-bearing mineral deposits (e.g., talc or vermiculite) are shown in **Figures D-4 (A) through (H).** These are images of unprocessed samples, i.e., from ores that had not yet undergone milling or any other processing to form powders. Nonetheless, many of these images show cleavage fragments or other elongate particles that could have resulted from attrition for which habit of growth appears to be ambiguous. Images further depicting potential ambiguity in determining growth habit of individual amphibole particles after processing of talc into finished products, are shown in ***Appendix F***.

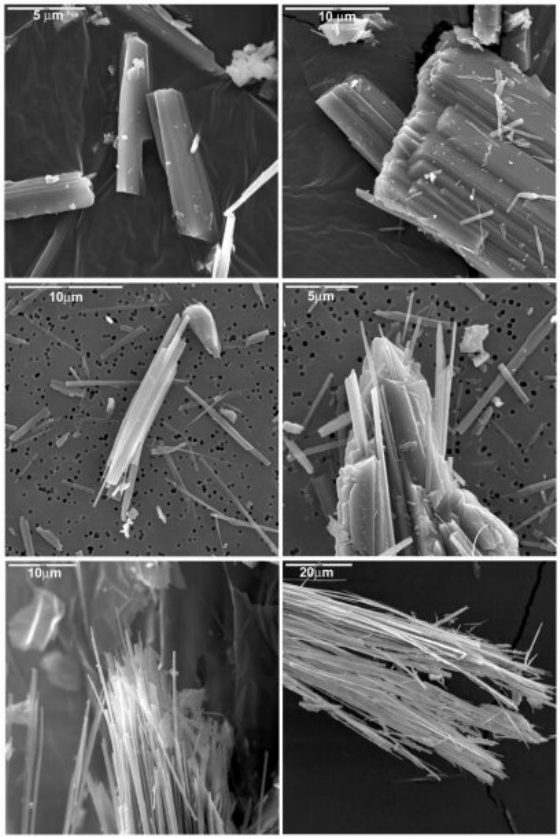


Figure D-4 (A). **Electron micrographs of typical morphological types of vermiculite amphiboles** showing variations in morphology of amphiboles in a commercial vermiculite deposit (Rainy Creek complex near Libby, Montana) mined from 1923 to 1990. The morphologies exhibited by these particles range from prismatic crystals (upper left) to asbestiform (lower right) with varying degrees of fibrous morphology exhibited between the extremes. (source: Meeker et al., 2003, https://libbyasbestos.org/wp-content/uploads/2016/11/Meeker-et-al.-2003.-The-Composition-of-Amphiboles-from-the-Rainy-Creek-Complex.pdf).

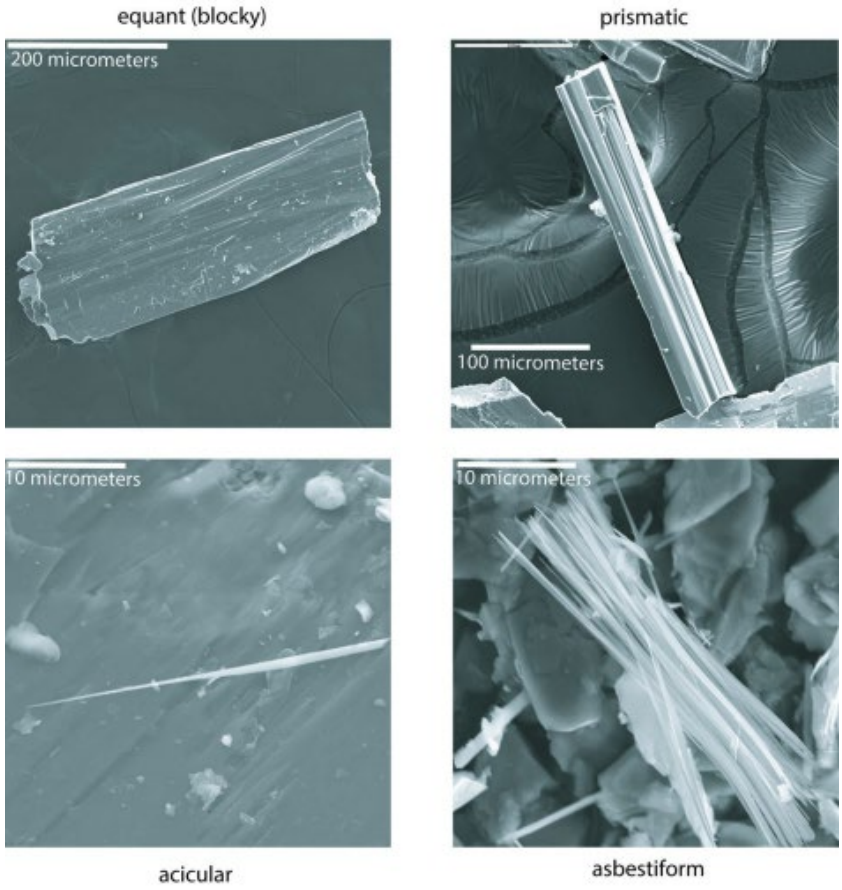
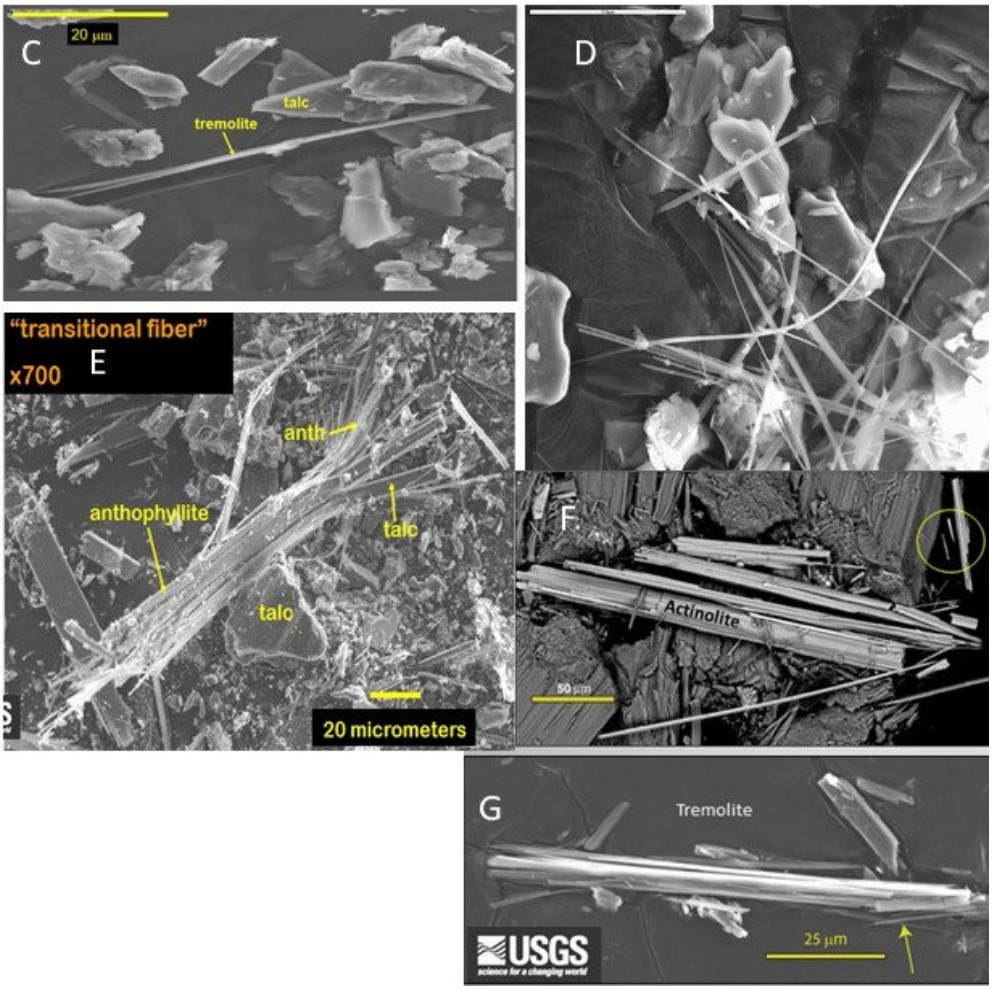


Figure D-4(B). SEM images showing variations in amphibole morphology within a region in Death Valley National Park in California where talc had been mined during the 20th century (source: Van Gosen, et al, 2004b, https://pubs.usgs.gov/of/2004/1092/OF-2004-1092_508.pdf).



Figures D-4 (C)-(G). SEM images showing variations in morphology of amphibole and complex amphibole-containing particles found in talc deposits. **Panel (C):** A structure of tremolite, dispersed among talc particles, which may be regarded as "tremolite asbestos" in that it appears to be separable into narrower fibers or fibrils along its length (source: presentation on "The Mineral Fibers of Potential Concern in Talc" by B.S. Van Gosen at JIFSAN "Asbestos in Talc Symposium" Nov. 28, 2018); **Panel (D):** Tremolite dispersed among talc may be regarded as "tremolite asbestos" in that it exhibits evidence of being flexible and appears to be separable into narrower fibers or fibrils along its length; **Panel (E):** A fibrous particle, referred to as "transitional", that is not identifiable as either anthophyllite or talc although evidence of both minerals is found in the same particle; the particle evidently resulted from an incomplete chemical change from anthophyllite to talc (source: USGS Denver Microbeam Laboratory https://www.usgs.gov/media/galleries/fibrous-and-asbestiform-minerals); **Panels (F) and (G):** Amphibole particles (actinolite and tremolite, respectively) some of which appear to be "fibrous", in the presence of particles that are "cleavage fragments" resulting from attrition along cleavage planes. **Panel D, F and G source:** presentation on "Mineral Fibers of Potential Concern in Talc – Geology and Mineralogy" by B.S. Van Gosen at FDA "Public Meeting on Testing Methods for Asbestos in Talc and Cosmetic Products Containing Talc", February 4, 2020).

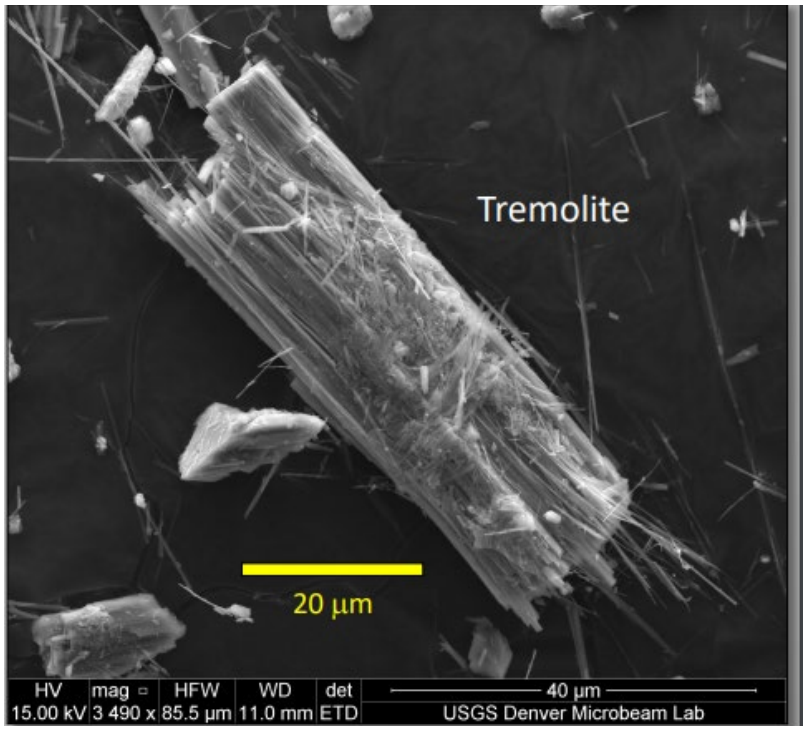


Figure D-4 (H). Tremolite particle that appears to show both habits of growth (asbestiform and non-asbestiform). (source: USGS Denver Microbeam Laboratory https://www.usgs.gov/media/galleries/fibrous-and-asbestiform-minerals)

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4. Other Relevant Resources

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29 CFR §1910.1001. Asbestos. *Code of Federal Regulations.* Title 29 (Occupational Safety and Health Administration), Part 1910: Toxic and Hazardous Substances. https://www.osha.gov/laws-regs/regulations/standardnumber/1910/1910.1001 (Date accessed 1/6/21)

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APPENDIX E: HEALTH-BASED CHARACTERISTICS TO ADDRESS IMPACTS OF ASBESTOS AND OTHER ELONGATE MINERAL PARTICLES IN TALC INTENDED FOR USE IN COSMETICS

1. Introduction

Asbestos is a known human carcinogen, and its health risks are well-documented. There is general agreement among federal agencies, most developed nations, and the World Health Organization (WHO) that there is no established threshold for health effects from asbestos exposure. Asbestos exposure by inhalation or ingestion can cause adverse effects ranging from inflammation to pleural disease, lung cancer, and mesothelioma. These effects are rarely seen acutely but are more likely to occur many months or years following exposure. Exposure to asbestos may also lead to the development of cancers in other parts of the body, remote from the sites of primary exposure, including cancers of the larynx, gastrointestinal tract, and ovaries.

The specific biological mechanisms underlying asbestos and other elongate mineral particle (EMP)[16] induced inflammation and/or disease in humans and other animals remain uncertain. Additionally, a more complete understanding of particle characteristics associated with activation of these biological mechanisms is lacking and will be essential to furthering our understanding of the toxicity of asbestos and other amphibole particles (Asgharian, Owen et al. 2018).

Historically, requirements for regulating exposures to asbestos in occupational settings were indexed based on a specified limited range of mineral types, particle sizes, and other characteristics that were defined to aid the efficiency and statistical reproducibility of particle counting. However, this practice under the phase contrast microscopy (PCM) method of indexing EMP characteristics, though useful in limited occupational settings, is inadequate for assessing exposure (Stanton M.F. and Layard 1981, Davis, Addison et al. 1991, Stayner, Kuempel et al. 2008, EPA 2010, Boulanger, Andujar et al. 2014). Decisions to limit elongate particle size definition to specific size fractions (e.g., length $\geq$ 5 µm; width $\geq$ 0.2 µm, and aspect ratio $\geq$ 3:1) were established for the convenience of using light microscopy to estimate exposures in occupational environments (Rooker, Vaughan et al. 1982). Thus, while it may be a useful index for exposure in certain situations, "the fiber counting protocol using a 3:1 aspect ratio and a length of 5 µm or greater as being in some way a definition of asbestos has no scientific basis." (Addison and McConnell, 2008). "The current PCM method is inadequate for assessing

[16] Elongate mineral particle (EMP) defined as *"any mineral particle with a minimum aspect ratio of 3:1."* (NIOSH 2011).

exposures to fibers in mixed-dust environments, and it lacks the capability to measure all the important physical and chemical parameters of EMPs thought to be associated with toxicity" (NIOSH 2011).

Particle size, tensile strength, morphology, chemical composition, bio-persistence, surface charge, surface porosity, and reactivity have all been implicated in the pathogenic processes associated with EMP exposure (HEI 1991). Our general understanding of the mechanisms and progression of EMP-related disease comes from studies about biophysical, cellular, animal, and human responses to exposure (NATO 1990, Fubini and Arean 1999, Xu, Zhou et al. 2002). Elongate particle interactions with cellular components can result in aberrations in cell division (Livingston, Rom et al. 1980, Achard, Perderiset et al. 1987, Renier, Levy et al. 1990, Korkina, Durnev et al. 1992), generation of reactive oxygen species (Brown, Fisher et al. 1998) and an inflammatory response (Shukla, Ramos-Nino et al. 2003, Mossman 2018, Pfau, McNew et al. 2019). Several studies in animal models report that longer fibers are more strongly associated with cancer incidence (Stanton M.F. and Layard 1981, Davis, Addison et al. 1991, Berman, Crump et al. 1995). Stanton and Layard (1981) demonstrated correlations with tremolite fibers longer than 8 µm with width less than 0.25 microns and particles greater than 4 µm in length with width less than 1.5 µm. In a study by Davis et al. (1991) exposure to short (< 5 µm) brittle tremolite fibers produced mesotheliomas in nearly 70 percent of the rats tested. Investigation of human exposures have demonstrated the debilitating and deadly consequences of EMP inhalation without conclusive attribution to specific particle sizes (Stayner, Kuempel et al. 2008, Naik, Lewin et al. 2017).

Particle size, aspect ratio (length-to-width ratio), dissolution characteristics, and cellular processes affect exposure. Additionally, anatomy and physiology of the host, internal distribution, retention, and clearance from the body are all determinants of internal exposure. (CDC/NIOSH 2011). When airborne EMPs are inhaled, both their aspect ratio and other aerodynamic characteristics (e.g., particle width, length, density, flexibility, and precession) determine where within the respiratory tract the particles are initially deposited. Generally, thinner particles with higher aspect ratios, may penetrate more deeply into the lungs (Timbrell 1982, Lippmann 1990, Bernstein, Rogers et al. 2011). Larger particles and those with higher density may impact the nasopharyngeal region of the upper airways, where they are more efficiently removed from the respiratory tract through mucociliary transport to the esophageal region and swallowed, causing exposure within the digestive system. Historically, requirements for recording occupational and non-occupational exposure to EMPs typically provide only

limited characterization of exposure materials. These limitations in dose characterization have contributed to an incomplete toxicological characterization of particle dose-response.[17]

Established as convenient exposure indices for the purpose of estimating occupational safety, these analytical methods were used with awareness that "*shorter fiber was the predominant component in air"* (Langer, Nolan et al. 1991). However, these censored exposure indices are not capable of, nor were intended to, be used in context of consumer exposure to the presence of asbestos in cosmetics.

2. Toxicology of elongate mineral particles

More than four decades ago (prior to the practice of indexing fibers), the CDC/NIOSH fully characterized the presence of EMPs (including subsets of regulated asbestos and asbestiform minerals), in a talc mining and milling operation in St. Lawrence County, New York; where morbidity and mortality was significant in workers exposed to dusts (NIOSH 1980). Milled talc samples contained 37-59% tremolite and 4.5-15% anthophyllite, while airborne concentrations of fibrous amphibole ranged from 9.5-17.5 fibers/cm^3 in the mine and 9.9-70.6 fibers/cm^3 in the mill. Using TEM, NIOSH characterized mineral fiber size distribution similar to those observed in other operations. The median fiber lengths for airborne tremolite and anthophyllite were 1.6 µm and 1.5 µm respectively while the respective median fiber widths were 0.19 µm and 0.13 µm. It was observed that 97% of the worker exposures to tremolite and 90-92% of the worker exposures to anthophyllite were to fibers <5 µm in length, well below the size range commonly recorded by less sensitive light microscopic techniques.

Once inside the body through inhalation, ingestion, or perineal exposure, EMPs can migrate through tissues and organs to secondary sites of exposure where progressive cell damage can occur (Cook and Olson 1979, Wehner 1994, Heller, Westhoff et al. 1996). It is a fundamental premise of EMP toxicology that the risks of irreversible damage to cells and tissues of the body following exposure are associated with the accumulation of elongate particles in susceptible tissues. Retention and accumulation of elongate particles in biological tissue is influenced by the nature of the EMP, magnitude of the exposure, host physiology, type of tissue, migration and transformation of particles within the body, and clearance of particles through cellular mechanisms, including dissolution and removal by alveolar macrophages. Thus, it is critical to obtain detailed characterization of particle populations to which individuals are exposed in order to understand their relevance and degree of contribution to disease.

[17] See Stayner, L., Kuempel, E., Gilbert, S., Hein, M. Dement, J., 2008. "An epidemiological study of the role of chrysotile asbestos fibre dimensions in determining respiratory disease risk in exposed workers" Occup. Environ. Med., 65(9): 613-619 https://oem.bmj.com/content/65/9/613.long; NIOSH (2011) Bulletin #62, p. 67, https://www.cdc.gov/niosh/docs/2011-159/default.html.

In rare cases where a broad characterization of fiber size distribution is made in environmental or biological matrices, the majority of fibers are often identified as shorter (less than 5 μm) than are presently regulated by OSHA (Timbrell 1982, Dodson, Atkinson et al. 2003, Suzuki, Yuen et al. 2005). It is generally well accepted that, when inhaled, longer and thinner mineral particles tend to be more fibrogenic and carcinogenic than shorter, thicker particles of identical chemical make-up (Stanton M.F. and Layard 1981, Berman, Crump et al. 1995), yet shorter elongate particles (>0.5 μm and <5 μm) clearly contribute to disease (Stanton M.F. and Layard 1981, Stayner, Kuempel et al. 2008, EPA 2010, Naik, Lewin et al. 2017). Given that fiber load in the lung is an important determinant of disease, elongate particles of all sizes contribute to the total surface area available for disturbance at the biological interface (Goodglick and Kane 1990). This is especially the case with chronic exposures when natural clearance mechanisms may be impaired or overwhelmed. Research findings of Stayner et al (2008) show that cumulative exposures to "*all fibre size indices, including fibres <5 um in length, were highly statistically significant predictors of lung cancer or asbestosis mortality*." (Stayner, Kuempel et al. 2008).

Comprehensive understanding of the physical nature and surface chemistry of elongate particles is often overlooked when estimating hazard. Together, many characteristics contribute to EMP toxicity, such as biological persistence, inter-tissue migration, or *in vivo* comminution (splitting of bundles into elongate fragments or fibers). Interactions of EMP at the biological interface can trigger intracellular multiprotein complexes associated with inflammation. In a study of internal exposure, Cook (Cook, Palekar et al. 1982) demonstrated the fate of a single dose of ferro-actinolite or amosite particles in rat lung over the course of 2 years. During this time, the internal fiber dose of ferro-actinolite increased more than 4-fold. This increase was presumably caused by comminution of EMPs within the lung that contributed to an increase of the internal dose over time (**Figure E-1**).

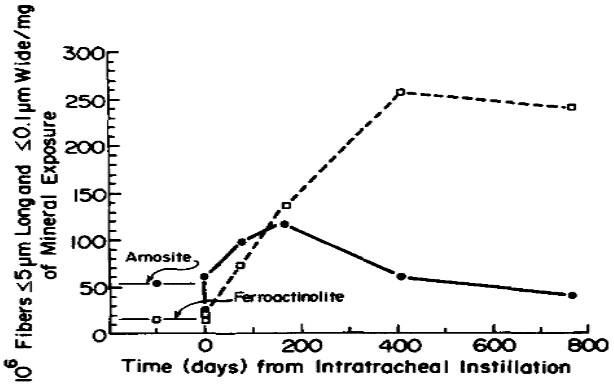

Figure E-1. Evidence that fibers may multiply in the lung following exposure. Research from Cook et al. (Cook, Palekar et al., 1982) shows tissue concentrations of ferroactinolite particles increase over time.

In vivo fiber-splitting would have increased both the fiber dose and reactive surface area available to cause cell damage and an inflammatory response. Particle surface area modulates chemical reactivity and is an important, but widely overlooked, metric for understanding differential chemical activation at the biotic interface (Fubini 1997).

3. The importance of fiber reactivity and morphology

A number of studies (Goodglick and Kane 1990, Dodson, Atkinson et al. 2003, Ji, Wang et al. 2012) report an association between fiber length, width, and disease in laboratory animals and in exposed human populations. However, the methods, definitions, and protocols used to measure and count fibers in environmental samples are not independent of the specific analyst or microscope used to characterize exposures (Rooker, Vaughan et al. 1982). Fiber visibility is a function of fiber length and width and many fibers that are too short or thin to be resolved by the commonly employed phase contrast or polarizing light microscopes may be missed (Kenny, Rood et al. 1987). Factors affecting fiber visibility include the visual acuity of the observer, the optical performance of the microscope, and the methods used to prepare the sample. The use of optical microscopy is convenient as an index of the presence of EMP but is not capable of identifying or characterizing pathogenic fibers smaller than the resolution of the optical microscope. Thus, for the purpose of toxicology, hazard identification and exposure-informed protection of public health, more advanced and comprehensive characterization of dose that is more independent of analyst's subjective judgment must be considered.

Evidence demonstrates that after respiratory exposures to talc or other EMP-contaminated dusts, short (<5 μm) EMPs represent the predominant fiber population found in biological tissues (Dodson, Graef et al. 2005, Boulanger, Andujar et al. 2014). For example, analysis of airborne EMP during federal response operations to the vermiculite mine-related amphibole exposures in Libby, Montana demonstrated a predominance of short particles. A majority of these 'Libby Amphibole' particles demonstrated morphologies and crystal structures inconsistent with the commonly employed mineral species and size limits (length and width) (**Figure E-2**) imposed by most federal regulations. Investigations by the French Agency for Food, Environmental and Occupational Health Safety (ANSES) and the US EPA are consistent with the expectation that fibers outside of the commonly recorded regulatory size limits often dominate airborne exposures (**Figure E-3**) (Rohl and Langer 1974, Boulanger, Andujar et al. 2014).

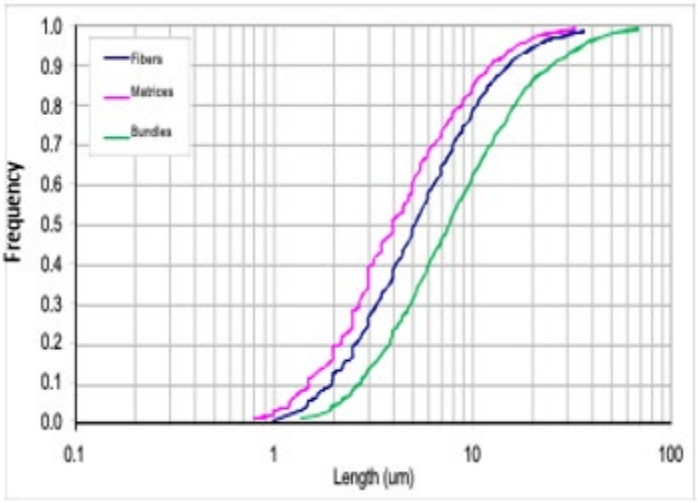

Figure E-2: Frequency distribution of 29,504 Libby Amphibole particles (fibers 81%, matrices 11%, and bundles 8%) collected on air filters in Libby, MT using TEM analysis method ISO 10312. Note that more than half of the exposure would not have been captured by standard analytical methods that only count particles with length ≥5 µm (EPA 2010).

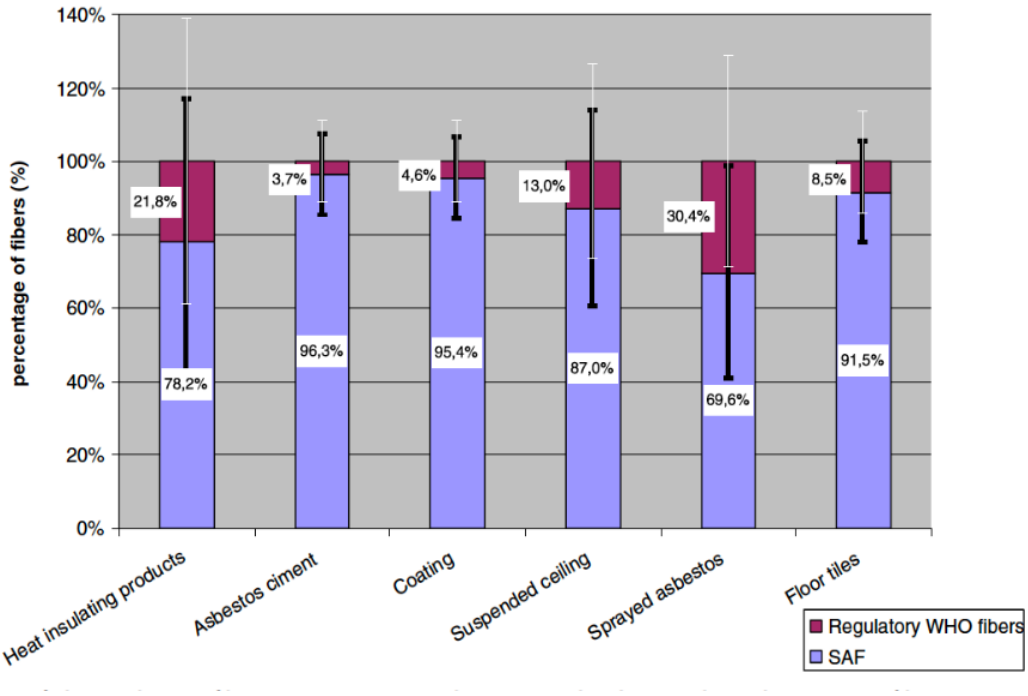

Figure E-3: Percentage of short fibers (SAF): L < 5 µm, d < 3 µm and L/d > 3 and regulatory WHO fibers: L ≥ 5 µm, d < 3 µm and L/d > 3, according to the type of asbestos containing materials (ACM), measured by TEM in 105 air samples obtained in 64 public buildings in Paris area, between 1997 and 2004, for asbestos regulatory diagnosis purposes. (Boulanger, Andujar et al. 2014).

In 2001, researchers (Suzuki and Yuen 2001) studied the morphology of asbestos fibers in the lung and pleura of human mesothelioma victims. Suzuki and Yuen (2001) found "[t]he majority of asbestos fibers detected in the lung and mesothelial tissues [81.4%; 2347/2884] were shorter than 5 µm in length". Short EMPs also predominate in the mesentery and omentum regions in the body where chronic perineal exposures to talc may occur (Dodson, Williams et al. 1990).

Alveolar macrophage cells play a critical role in the removal of inhaled particulates from the lung by the process of phagocytosis (Krombach, Munzing et al. 1997). When these cells are overwhelmed by large numbers of fibers in the lung or encounter particles too long to engulf (longer than their approximate diameter of 20 µm), their ability to capture and clear particles from the lung is diminished. Although shorter particles are generally more rapidly cleared than longer ones, at a steady state of exposure, short EMPs can accumulate, presenting a persistent and much larger bioactive surface area than the commonly recorded longer fibers (Lehnert, Valdez et al. 1989). The inhibition of cellular phagocytosis due to such fiber overload, coupled with the presence of longer fibers, can initiate a series of events leading to inflammation and fibrotic disease (Pfau, McNew et al. 2019). Thus, under chronic exposure conditions, short fibers inhibit the lung's natural clearance mechanisms and provide greater potential for interaction at the biological interface, increased generation of reactive oxygen species (ROS), and activation of cellular inflammatory responses leading to fibrosis. While the inflammasome[18] can be activated by a number of endogenous and exogenous signals, iron (present in many EMPs), is a catalyst for the formation of ROS and is suspected to play a role in inflammation (Hardy and Aust 1995, Kane 1996). For example, when hamsters were exposed (0.15, 0.75, and 3.75 mg/100 g body weight) for 1-14 days to talc that was collected from worksites and presumed to be "asbestos-free," elevated protein levels, edema, and increased cell counts (by broncho-alveolar lavage) were observed. However, phagocytosis by macrophages was inhibited by talc dust and this inhibition may contribute to reduced clearance of EMPs (Beck, Feldman et al. 1987). Many studies indicate the amelioration of cell damage and cell activation when ROS scavengers and anti-oxidants are introduced following exposure to EMPs (Goodglick and Kane 1990). This implies that ROS may play an important role in inflammation and disease associated with elongate particle exposure.

4. Summary

When comprehensive dose characterization has been available, biologically active EMPs, also known as censored EMPs (i.e., < 5 µm in length), are often implicated as contributing to disease. These EMPs have been frequently removed from the exposure analysis due to the limitations of optical microscopy. Further, our understanding of disease in relation to exposure (exposure-response analysis) is severely limited. The presence of elongate amphibole and serpentine

[18] The **inflammasome** is a multiprotein intracellular complex that detects pathogenic microorganisms and sterile stressors, and that activates the highly pro-inflammatory cytokines interleukin-1b (IL-1b) and IL-18.

minerals in some talc deposits has been known for many years (Kleinfeld, Messite et al. 1967, Rohl and Langer 1974, NIOSH 1980), yet analytical methods restricted by available technology (Rooker, Vaughan et al. 1982, Kenny, Rood et al. 1987) and developed for other purposes, have been adopted as tools for the scientific characterization of toxicological response and risk assessment in both occupational and non-occupational epidemiologic studies. This has severely limited our understanding of how exposure to EMPs of various size and characteristics contribute to asbestos-related disease (Stayner, Kuempel et al. 2008) (**Figure E-4)**.

Thus, for the purpose of evaluating the presence of asbestos in talc intended for use in cosmetics and talc-containing cosmetics, measurement and characterization of EMPs should be more inclusive in order to consider biologically relevant physical-chemical characteristics as they relate to biological actions of the offending mineral particles. Such analytical protocols should free the analyst from a subjective role in the reporting of results and will further aid in our ability to understand the health impact from exposure to a variety of different asbestos particles.

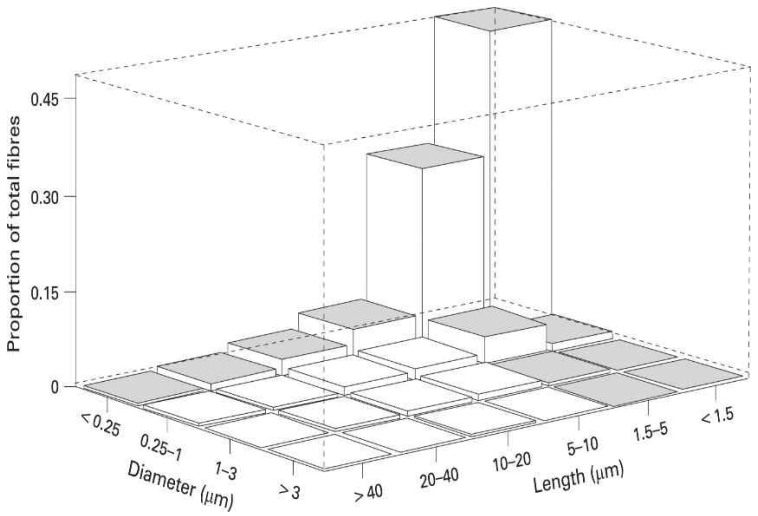

Figure E-4: Fibers shorter than 5 µm have traditionally not been counted by methods used for regulatory standards for asbestos because these methods were developed to provide a reproducible index of fibre exposure. The findings from this analysis show that cumulative exposures to "*all fibre size indices, including fibres <5 um in length, were highly statistically significant predictors of lung cancer or asbestosis mortality*." (Stayner, Kuempel et al. 2008)

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APPENDIX F: TESTING ISSUES

1. Comparison of Published Standards for Monitoring the Quality of Talc

Currently, each of the published quality standard methods for talc as an ingredient in cosmetics, drugs, and foods contains different criteria for certifying that asbestos is not present. These standard methods include: 1) the CTFA (now known as the PCPC) specification titled "Asbestiform Amphibole Minerals in Cosmetic Talc"; 2) the United States Pharmacopeia (USP) monograph titled "Talc" for "Absence of Asbestos"; and 3) the FCC monograph titled "Talc FCC." Refer to **Table F-1** for more information on the content of these standards. By contrast, there currently are no public market standards for quality of industrial-grade talc, and commercial grades marketed as "talc powder" that may contain as little as 30% talc (NIOSH, 1980; Kelse and Thompson, 1989; IARC, 2010). Consistency with official compendia (e.g., the USP) for talc used as a component in drugs is mandatory under the Federal Food, Drug, and Cosmetic Act (FD&C Act)). The USP standard can also be used to certify talc for other purposes, including cosmetics. While the edition of the FCC standard that applies to the listings of talc as generally recognized as safe does not include talc (21 CFR 170.30(h)(1)); the more recent edition of the FCC includes specifications for food grade talc. The cosmetic industry quality standard for talc is voluntary and has not been updated since 1976 (CIR 2013).

The CTFA J4-1 and USP methods remain the only published test methods for asbestos in talc used in cosmetics and pharmaceuticals, respectively, despite long-recognized shortcomings in their specificity and sensitivity when compared with electron microscopy-based methods (see Millette, 2015; and Block et al. 2014) (see **section F.2**). The FCC standard for food grade talc does not provide a method for asbestos analysis but merely requires that talc for use in food NOT be from mines "known to contain asbestos" (FCC, 2019).

Although currently, there are no published talc quality standards that include electron microscopy methods for asbestos-testing, the utility of TEM is acknowledged by the cosmetics industry in its CTFA J4-1 method and by experts currently developing new talc-asbestos testing methods in parallel within two standards development organizations, USP[19] and ASTM.[20]

[19] See https://www.uspnf.com/notices/talc-nitr-20200731.
[20] See https://www.astm.org/DATABASE.CART/WORKITEMS/WK30039.htm.

Table F.1 – Comparison of Published Testing Methods for Asbestos in Talc

Standard Method	Definition or Description of Talc in the Method	Title of Requirement/ Method for Asbestos	Technique for Asbestos Analysis
Cosmetic Talc[1]	Cosmetic talc is an essentially white, odorless, fine powder, ground from naturally occurring rock ore. It consists typically of 90% hydrated magnesium silicate, with the remainder consisting of naturally associated minerals such as calcite, chlorite, dolomite, kaolin and magnesite, and containing no detectable fibrous, asbestos minerals. It conforms to the formula: $Mg_6[Si_8O_{20}] \cdot (OH)_4$.	*Asbestiform Amphibole Minerals in Cosmetic Talc (Method J4-1)*	Procedure 1: XRD Procedure 2: PLM only performed if XRD is positive for amphibole.
Talc USP[2]	Talc is a powdered, selected, natural, hydrated magnesium silicate. Pure talc has the formula $Mg_3Si_4O_{10}(OH)_2$. It may contain variable amounts of associated minerals among which chlorites (hydrated aluminum and magnesium silicates), magnesite (magnesium carbonate), calcite (calcium carbonate), and dolomite (calcium and magnesium carbonate) are predominant.	*Absence of Asbestos*	Procedure 1 or 2: Lab has option to use either XRD or IR Procedure 3: optical microscopy only performed if XRD or IR is positive for amphibole or serpentine.
Talc FCC[2]	Talc occurs as a white to gray-white, unctuous powder. It is a naturally occurring form of hydrous magnesium silicate containing varying proportions of such associated minerals as alpha-quartz, calcite, chlorite, dolomite, kaolin, magnesite, and phlogopite. *Talc derived from deposits that are known to contain associated asbestos is not food grade*. It is insoluble in water and in solutions of alkali hydroxides but is slightly soluble in dilute mineral acids.	See description.	No method provided.

[1] Information obtained from the Cosmetic Ingredient Specification for Talc (Ingredient ID# 3119), Personal Care Products Council (PCPC), Revision Date: 10/12/1989. The following statement, including a disclaimer, provided to FDA by PCPC in an email from J. Nikitakis on 7/29/2020, refers to the source, an online index of specifications for cosmetic ingredients. *"This index lists methods that were formerly published in the CTFA Compendium of Cosmetic Ingredient Composition (1990). The methods were developed by an industry committee of analytical chemists charged with the task of creating chemical specifications for cosmetic ingredients. Analytical methods were developed when existing suitable methodology was not available in other relevant compendia (e.g., USP, FCC). Users should be aware that these methods were last published in 1990 and are included in the On-Line for informational purposes. Other more current analytical techniques may be more suitable, and usage of any method listed herein is at the discretion of the user."*

[2] The United States Pharmacopiea (USP) and Food Chemicals Codex (FCC) specifications are public standards available by subscription. From USP and FCC specifications, both of which were downloaded on 11/5/2020 and 7/29/2020, respectively.

The criteria for quality in all three published standards collectively suggest that talc intended for use in FDA-regulated products is of relatively high purity, substantially consists of flat (platy) particles, and lacks appreciable amounts of particles with other shapes that could adversely affect talc quality. However, the published standards do not prescribe intervals at which talc should be tested or sampling plans to ensure absence of asbestos, and only provide limited assurance that the talc is not contaminated with asbestos.

Talc used as a raw material to manufacture cosmetics may routinely contain up to 10% accessory minerals (IARC, 2010). Talc for use in cosmetics appears to be essentially free of transition metal elemental impurities that can impart color. Levels of magnesium-containing accessory minerals (e.g., magnesium carbonate, chlorite, tremolite, anthophyllite, chrysotile) are not controlled through any test method in the specification. The assay for talc is merely an assay of total magnesium and thus is not necessarily indicative of the talc purity. The tests for asbestos in cosmetic and pharmaceutical grades of talc raw materials are shown below:

CTFA Method J4-1 for Asbestiform Amphibole Minerals in Cosmetic Talc

Method J4-1 is a private standard issued by Personal Care Products Council (previously known as Cosmetic Toiletries and Fragrances Association - CTFA) published in 1976. This standard has not been updated since that time. Permission to reproduce J4-1 here was provided to FDA by PCPC in an email from J. Nikitakis on 7/29/2020.

Asbestiform Amphibole Minerals in Cosmetic Talc

Part I: X-ray Diffraction Method

Part II: Optical Microscopy and Dispersion-Staining Method

Introduction

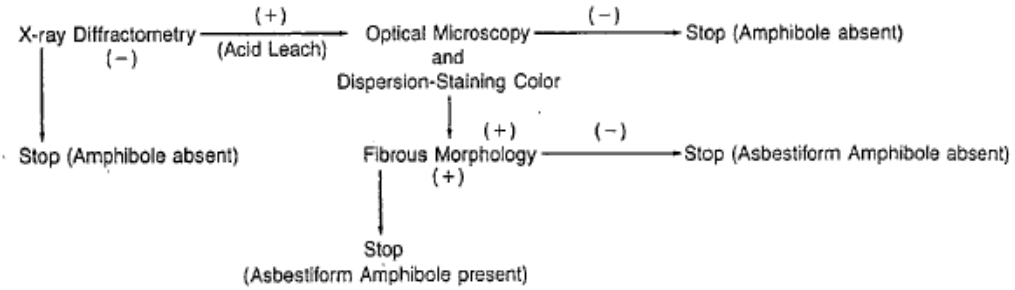
The method which has been adopted for the detection of amphibole minerals in cosmetic talc is the generally accepted method of x-ray diffraction. Methods which appear in the literature for the detection of fibrous amphibole, such as transmission electron microscopy with selected area diffraction[1] and electron microprobe,[2] have also been considered since they are capable of a lower level of detection than by x-ray diffraction. However, they have not been adopted since they suffer from the drawbacks, that the amount of material under examination is quite small (less than a microgram) and the time for analysis, expertise required, and expense of equipment eliminates them as routine methods.

The methodology presented is the most practical available, based on current technology. The use of Transmission Electron Microscopy with Selected Area Electron Diffraction offers greater sensitivity, but is not presented since it is unsuitable for normal quality control application.

Enrichment or concentration techniques using flotation cells have been tried as a means of improving the detection level; however, all efforts so far have been unsuccessful.

Principle

The x-ray diffraction method is based upon the principle that when a crystalline material is placed in an x-ray beam, a portion of the x-rays are diffracted by each set of atomic planes within the crystal. The diffracted rays strike a scintillation counter as the sample is scanned through a prescribed angle with the resulting development of peaks corresponding to each interplanar distance (d). A peak with d value in the range of 8.04 to 8.85Å for a sample talc is strong evidence for the presence of amphibole in that talc. The level of detection of amphibole by this method is 0.5% and above. The variability of detection is caused by such factors as age and manufacturer of x-ray diffractometers, sample homogeneity, specific amphibole mineral present, morphology of amphibole, particle size, preferred orientation, etc. For these reasons the level of detection should be reported for levels above 0.5%, since below this level the data has been found to be not reproducible. If a statistically significant peak is found of intensity equal to or greater than that obtained for the 0.5% standard in the d range for amphibole, described above, then the sample must be put through the following confirming scheme:



Part I: Amphibole Minerals by X-ray Diffractometry

Apparatus

1. X-ray diffractometer, employing nickel-filtered copper K-α radiation, horizontal or vertical goniometer with variable scan speed capability, suitable talc pellet sample holder, variable speed recorder, electronic panel including ratemeter and variable attenuation and time constant settings
2. Hydraulic press, capable of attaining a pressure of 15,000 to 24,000 lb calculated on a 3" ram
3. Mortar and pestle or grinding mill (Note 1)
4. Waring Blendor,* or equivalent blender
5. Spex Mixer/Mill,* or equivalent mechanical mixer
6. Sieve, 325-mesh
7. Optical microscope (Note 2)
8. 1¾" pellet press

Reagents

1. Standard talc sample, containing no detectable amphibole minerals
2. Standard tremolite sample, at least 80% pure
3. Denatured ethanol
4. Boric acid

Procedure

The procedure consists of slow-scanning, under previously determined conditions, a compressed pellet of the sample talc in the 11.0 to 10.0°2θ (8.85 to 8.04 Å) region for the presence of an amphibole peak. There are times when it is difficult to discriminate a possible peak for amphibole over the background noise level.

Should the presence of a small amphibole peak above the background "noise" be in question, it will be necessary to statistically evaluate the scan. A timer/scaler is required on the electronic panel of the x-ray diffractometer. In order for a peak to be statistically significant, the peak intensity must equal or exceed three standard deviations (3σ) above the average background intensity (N):

*Registered Trademark

Where $N + 3\sigma$ = minimum peak intensity
N = average background count
$\sigma = N$

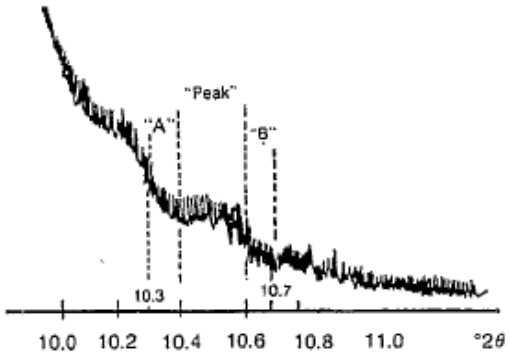


Figure 1.

Determine the region of the scan in question: in the Figure 1 scan, a peak appears to be present in the 10.40 to 10.60°2θ region.

Slow scan with cumulative pulse counting through the peak region three separate times and average the number of counts.

Determine a background count by scanning a region equal to ½ of the °2θ region covered by the peak, immediately, before and after the peak. The counting time for each of these background regions will equal ½ the total counting time used for the peak. Count each background region three times. Then average each region and add the two averages to obtain the background count (N).

Example:

In Figure 1.

	Region (°2θ)	*Time (sec.)*
Peak	10.40 to 10.60	120
Background		
Region A	10.30 to 10.40	60
Region B	10.60 to 10.70	60

Peak 10.40 to 10.60°2θ		*Background* *Region A* 10.30 to 10.40°2θ		*Region B* 10.60 to 10.70°2θ	
time secs.	*counts*	*time secs.*	*counts*	*time secs.*	*counts*
120	60,332	60	28,784	60	28,506
120	59,870	60	28,943	60	28,368
120	60,105	60	28,634	60	28,204
Average	60,102		28,787		28,359

$$N = 28{,}757 + 28{,}359 = 57{,}146$$
$$\sigma = \sqrt{57{,}146} = 239 \quad 3\sigma = 717$$
$$N + 3\sigma = 57{,}146 + 717 = 57{,}863$$

The actual number of counts obtained for the integrated peak intensity was 60,102; therefore, the "suspect" peak is statistically present in the scan.

Standard Preparation

Optimal instrument conditions must first be determined with the use of tremolite standards: 1.0%, 0.75%, 0.5% tremolite by weight, prepared in a standard talc which is free of interfering peaks in the 11.0 to 10.0°2θ region.

Weigh out appropriate amounts of standard talc and tremolite both of which have been ground to pass a 325-mesh sieve. Transfer to a Waring Blendor.* Add 100 ml of ethanol to the blender and blend at low speed for 5 minutes.

Carefully transfer the contents of the blender, with repeated ethanol washings, into a large beaker. Evaporate the ethanol on a steam bath.

Shake the sample in a plastic vial for 5 minutes on a Spex Mixer/Mill* to remove clumps and caked sample resulting from the evaporation of ethanol.

Determine by microscopy the homogeneity of the prepared standard previous to the x-ray diffraction analysis.

Press the homogeneous standard into a 1¼" pellet with a backing of boric acid. Transfer 2 (±0.2) g of standard to the die-holder and evenly distribute on a polished, scratch-free die. Distribute 4 (±0.2) g of boric acid evenly on the talc layer. Press the mixture into a pellet under conditions suitable for obtaining a smooth planar surface (for example, a pressure of 15,000 to 24,000 lb calculated on a 3" ram has been found to produce suitable pellets). The resulting pellet must have a talc face which is free of flaws; if not, the pellet must be discarded (Note 3). Prepare two acceptable pellets from each standard.

*Registered Trademark

Sample Preparation

Prepare two pellets from each sample in the manner described for the standard pellets. Make a qualitative scan from 4 to 50°2θ on one of these pellets to ascertain the presence of amphibole above the 2% level or the presence of mineral impurities having interfering peaks in the 11.0 to 10.0°2θ (8.85 to 8.04 Å) region of the scan. The presence of such interference will eliminate use of the x-ray diffraction method for the sample, and one will have to proceed directly to the microscopical procedure.

Instrumentation

Instrumental variables are optimized on the 1% standard. Lower standards are then analyzed under the optimum conditions to determine the lower level of detection. Of major importance in obtaining maximum instrument sensitivity are a slow diffractometer speed combined with compatible recorder speed, and high attenuation combined with a statistically acceptable time constant on the ratemeter. Under appropriate instrumental conditions the peak obtained for the 0.5% standard should be detectable above background noise as shown in Figure 2.

Typical instrumental conditions employed for the Siemens Diffractometer (Model No. M386-X-A4), and Counter and Recorder Unit (Type T) are:

Radiation:	Cu with K_b filter at 40 KV and 24 ma
Divergence slit:	1° Receiving slit: 0.2 mm
Goniometer speed:	$^1/_{10}$°2θ/minute
Recorder Speed:	300 mm/hour
Attenuation:	1 x 10^3 impulses/second
Time constant:	T(s) = 4

Statistical error of 1.1% under these conditions

Rise Time = 0.18
Attenuator = 20

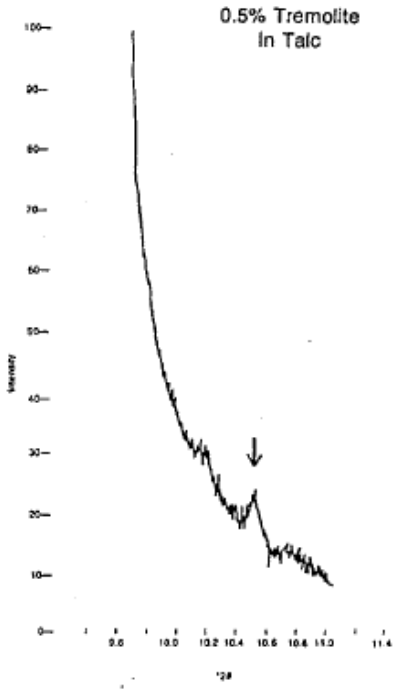


Figure 2

X-Ray Diffraction Scans

Place the standard or sample pellet in a suitable holder and slowly scan between 11.0 and 10.0°2θ. Then rotate the pellet 90° with respect to its original position in the goniometer and rescan between 11.0 and 10.0°2θ since pellet orientation may affect peak intensity. The presence of a reproducible peak (or peaks) is due to the presence of amphibole mineral (or minerals); the absence of peaks in this region indicates the absence of amphibole in the sample, within the limit of detection of this technique.

Report results as "None detected" or as "Detected approximately X% level," where "X" equals the level detected.

Part II: Asbestiform Amphibole Minerals by Optical Microscopy and Dispersion-Staining

Apparatus

1. Polarizing microscope. Best results will be obtained if the instrument includes the following:
   a. Individually centering objectives
   b. Bertrand lens
   c. High-intensity light source
   d. Centering condenser/substage
2. Dispersion-staining device (Note 4)
3. Vacuum filtration equipment, including either a porcelain cone with glass fiber filter mat or a porous glass bottom cup

Reagents

1. Hydrochloric acid, 10% v/v
2. Cargille immersion liquid Series HD, $n_D^{25^\circ} = 1.605$ (Note 5)

Procedure

Acid Treatment

Because of the interference caused by some carbonates (e.g., calcite) in the detection of asbestiform amphiboles in talc by optical microscopy/dispersion-staining, it is necessary to first remove these carbonates by a simple acid leaching procedure:

Weigh out 2 g of the talc into a 100 ml beaker. Add 25 ml of 10% v/v HCl slowly (to prevent excessive evolution of gas if carbonates are present) and heat, with occasional stirring on a steam bath for 30 minutes.

Filter with vacuum filtration equipment, and wash several times with hot water. Dry the talc.

Optical Microscopy and Dispersion-Staining

Carefully disperse 0.1 mg of talc in one drop of Cargille HD liquid, $n_D^{25^\circ} = 1.605$, and cover with a clean cover slip.

Examine the sample in the dispersion-staining central stop mode. The substage diaphragm should be almost completely closed, the field diaphragm may be partially closed to enhance color contrast, and the polarizer should be in position.

Tremolite, actinolite and presumably other amphibole minerals, under these conditions, will show the following dispersion-staining colors: yellow changing to blue with rotation of the sample relative to the polarizer *or* yellow changing to orange with rotation. The variation of the color change is due to the fact that the tremolite may lie in one of two positions relative to its principal optical orientation.

Examine the sample for asbestiform fibrous amphibole minerals.

In order for an amphibole mineral to be considered asbestiform fibrous it must meet the following OSHA definition (Reference 4).

1. Particles must appear to be fibrous rather than as crystals or slivers.
2. The maximum diameter of a fiber to be counted in 3 microns.
3. The maximum length of a fiber to be counted in 30 microns.
4. The length to width ratio must be 5 or more to 1, that is, 5 times or more longer than wide.
5. The separate or individual fibers must contain fibrils or the "bundle of sticks" effect, unless they are at a nondivisible stage. A fibril cannot be subdivided and would be counted, if it meets the other criteria. The length to width ratio of 5 or more to 1 is not meant to imply that other particles are not hazardous.

Report results as "Asbestiform Amphibole Present" or as "Asbestiform Amphibole Absent."

It is imperative that both dispersion-staining color *and* fibrous morphology criteria be satisfied before identifying a particle as asbestiform amphibole, since other substances may show colors similar to those described.

Notes

1. Talcs to be analyzed and the tremolite used to prepare standard samples must be finer than 325 mesh (maximum particle size of 44 microns). The Tekmar Analytical Mill (Model A-10) is available from:

   Tekmar Company
   P.O. Box 37202
   Cincinnati, Ohio 45222

2. It is important that the homogeneity of the prepared talc-tremolite standard samples be verified by optical microscopy.
3. This requirement is critical since excessive surface scatter will cause abnormally high background count.
4. The only commercially available dispersion-staining device is available from:

   Walter C. McCrone Associates, Inc.
   2820 South Michigan Avenue
   Chicago, Illinois 60616

5. Available from:

   R. P. Cargille Laboratories, Inc.
   Cedar Grove, New Jersey 07009

   —or from laboratory suppliers.

References

1. Rohl, A. N., Langer, A. M., *Environmental Health Perspectives 9*, 95 (1974)
2. Rubin, I. B., Maggiore, C. J., *Environmental Health Perspectives 9*, 81 (1974)
3. L. S. Birks, X-Ray Spectrochemical Analysis, pages 54–55, Interscience Publishers (1959)
4. "Tremolite and Talc." U. S. Department of Labor, Occupational Safety and Health Administration, Field Information Memorandum #74-92, November 21, 1974

* * * * *

The Cosmetic, Toiletry and Fragrance Association

Talc USP Test for Absence of Asbestos (downloaded 11/5/2020). Permission to reproduce from USP 43-NF 38 received via email on 8/10/21 from R. Lew, USP, to S. Wolfgang, FDA.

• **ABSENCE OF ASBESTOS**

[NOTE— Suppliers of Talc may use one of the following methods to determine the absence of asbestos.]

Proceed as directed for *Procedure 1* or *Procedure 2*. If either test is positive, perform *Procedure 3*.

Procedure 1: Infrared Absorption

The IR absorption spectrum of a potassium bromide dispersion of Talc at the absorption band at 758 ± 1 cm^{-1}, using scale expansion, may indicate the presence of tremolite or chlorite. If the absorption band remains after ignition of the substance at 850° for at least 30 min, it indicates the presence of tremolite. In the range 600 cm^{-1} to 650 cm^{-1} using scale expansion, any absorption band or shoulder may indicate the presence of serpentines.

Procedure 2: Use the following conditions (see *X-Ray Diffraction* ⟨941⟩):

Cu Kα monochromatic 40 kV radiation, 24–30 mA; the incident slit is set at 1°; the detection slit is set at 0.2°; the goniometer speed is 1/10° 2θ/min; the scanning range is 10°–13° 2θ and 24°–26° 2θ; the sample is not oriented. Prepare a random sample, and place on the sample holder. Pack and smooth its surface with a polished glass microscope slide. Record the diffractograms: the presence of amphiboles is detected by a diffraction peak at 10.5 ± 0.1° 2θ, and the presence of serpentines is detected by diffraction peaks at 24.3 ± 0.1° 2θ to 12.1 ± 0.1° 2θ.

Procedure 3: The presence of asbestos (see *Optical Microscopy* ⟨776⟩) is shown if there is a range of length to width ratios of 20:1 to 100:1, or higher for fibers longer than 5 µm; if there is a capability of splitting into very thin fibrils; and if there are two or more of the following four criteria: (1) parallel fibers occurring in bundles, (2) fiber bundles displaying frayed ends, (3) fibers in the form of thin needles, and (4) matted masses of individual fibers and/or fibers showing curvature.

2. Testing Issues (Limited Sensitivity/Specificity of Conventional Methods)

Testing for asbestos and other amphibole particles in talc and talc-containing cosmetics is especially challenging because of the different types of matrices sampled, the variable dimensions and shapes of the particles to be characterized, and the relatively low concentrations expected to be present. Thus, multiple methods of analysis are needed to provide an unequivocal identification of asbestos and other amphibole mineral particles of interest as previously noted, **(*Appendix F.5*)**.

When the first asbestos regulations were promulgated by OSHA and EPA, mandatory test methods only involved light microscopy. Since that time, electron microscopy methods have gradually been implemented to augment those less sensitive methods (see OSHA Method ID-191 on workplace regulation). Published light and electron microscopy techniques are now routinely applied by accredited asbestos testing laboratories to analyze samples of talc and talc-containing cosmetic products. However, modifications in the application of published protocols to include methods of sample preparation and definitions of asbestos and instructions for quantifying asbestos governing particle identification/reporting may differ among laboratories. Light microscopy is generally expedient and sufficient for detecting asbestos present at ≥1%, i.e., to ascertain if a bulk sample is an asbestos containing material (using PLM) or to monitor the amount of fibers released from materials into the air from asbestos containing materials (using PCM). However, the limited sensitivity of light microscopy reduces utility for detecting asbestos

in talc or cosmetic products where it may be present at several orders of magnitude less than 1% by weight.

Regarding test method specificity, PLM has some limited capability for mineral identification taking advantage of differences in the optical properties of minerals. Regarding sensitivity, as indicated by the description of asbestos in the EPA 600/R-93/116 protocol for bulk materials, PLM may be suited to detecting asbestos bundles in talc or cosmetics. PCM cannot be used for mineral identification and thus has no apparent applicability to testing of talc or cosmetics. PLM has limited ability to resolve structures that are <5 µm in length and/or where any dimension of the particle is below approximately 0.2 µm. This can lead to underreporting or false negative findings, especially when testing a talc-containing cosmetic product that has been milled and processed.

The published analytical methods for testing asbestos in cosmetic grade talc (CTFA J4-1) and pharmaceutical grade talc (Talc USP monograph) have similar shortcomings in sensitivity that can give rise to false negative results. Both dictate an approach that starts by screening for presence of signature diffraction patterns using XRD that indicate the presence of amphiboles (J4-1 and USP) and/or serpentines (USP).[21] However, XRD typically cannot detect the presence of amphiboles at less than 0.5% and is unlikely to detect serpentine (chrysotile), especially if chlorite is present, due to interference. In the J4-1 method, analysts are directed to use PLM to determine if asbestiform amphibole is present only when XRD testing is positive. Similarly, in the USP method, optical microscopy is used only if XRD or IR provides a positive finding for amphibole or serpentine. Thus, given the dimensions of asbestiform fibers and the inverse square relationship between fiber mass and fiber width, talc could conceivably contain up to billions (10^9) of asbestiform fibers per gram of talc and still be certified as being negative for asbestos (Rohl et al. 1974). These shortcomings and associated concerns with the current methods for asbestos-testing of talc have been discussed by Talc USP expert panel members (Block et al. 2014). Millette (2015) has also summarized the history of talc testing methodology for asbestos and similarly stated the inferiority of light versus electron microscopy methods. In conclusion, many scientists, including asbestos SMEs from the IWGACP, advocate for electron microscopy (TEM and SEM) to test talc for asbestos even if testing by light microscopy (and XRD) is negative (Rutstein et al. 2020; Millette, 2015), because a negative finding by PLM is not definitive for concluding that asbestos is not present.

The limitations of sensitivity and resolution can significantly reduce PLM utility when testing a solid material in which levels of asbestos are less than 1% by weight (**Figure F-1)**. Many publications indicate that the limit of resolution of PLM is ≥0.2 µm based on the fundamental

[21] Talc USP allows for the use of IR spectroscopy to screen for presence of amphibole/serpentine minerals as an alternative to XRD. IR and XRD have similar shortcomings in sensitivity and inability to determine morphology.

physics of light. These shortcomings become evident when a group of samples that have consistently tested negative for asbestos by PLM are found to contain asbestos by electron microscopy.

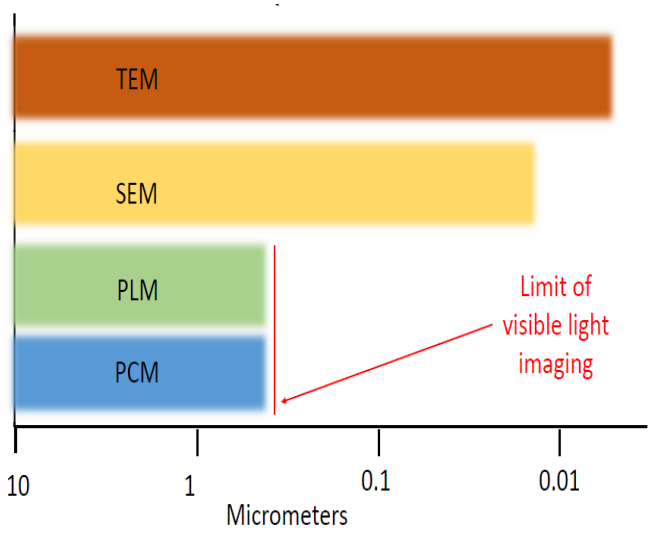


Figure F-1: Limitations of Light Microscopy for Detection of Fine Asbestiform Fibers. This figure depicts the approximate limits of resolution of visible light-based microscopes (PCM, PLM) and electron-based microscopes (TEM, SEM). Light microscopes are limited in theoretical resolution to approximately 200 nm (0.2 µm) due to the smallest wavelength of the illuminating visible light (~400 nm) and according to Abbe's equation. Electron microscopes have a theoretical resolution of much less than 0.1 nm; however, in practice, resolution is approximately 0.1-0.2 nm (0.0001-0.0002 µm) due to aberrations and distortions.

Data from a 2019 analysis of 52 cosmetic products[22] for the FDA highlights the potential for false negative findings when using PLM of samples containing low levels of chrysotile and tremolite particles. Of the nine samples that tested positive for tremolite and/or chrysotile by TEM/SAED/EDS, no asbestos was detected in seven samples (each sample was tested in triplicate) using PLM. **Figure F-2** shows the size distribution (width vs. length) of tremolite particles detected in one cosmetic products from this series. The majority of particles detected were less than 5 µm in length (as indicated by the vertical red lines at 5 µm) (many are also less than 1 µm in width). Similar profiles were found in most of the remaining samples. These findings clearly demonstrate the limitations of PLM and illustrate the need to use TEM to determine if asbestos is present in a cosmetic, and to obtain a complete understanding of the characteristics (morphology and mineral types) in the population of pertinent particles.

[22] See FDA Summary of Results from Testing of Official Samples of Talc-Containing Cosmetics for Asbestiform Fibers by AMA Analytical Services, Inc. (AMA) During Fiscal Year 2019, available at: https://www.fda.gov/media/135911/download and https://www.fda.gov/media/122414/download; and for example, AMA Analytical Services, Inc. Summary of Asbestos and Talc Analysis (PDF - 2MB) April 30, 2019; available at https://www.fda.gov/media/127825/download.

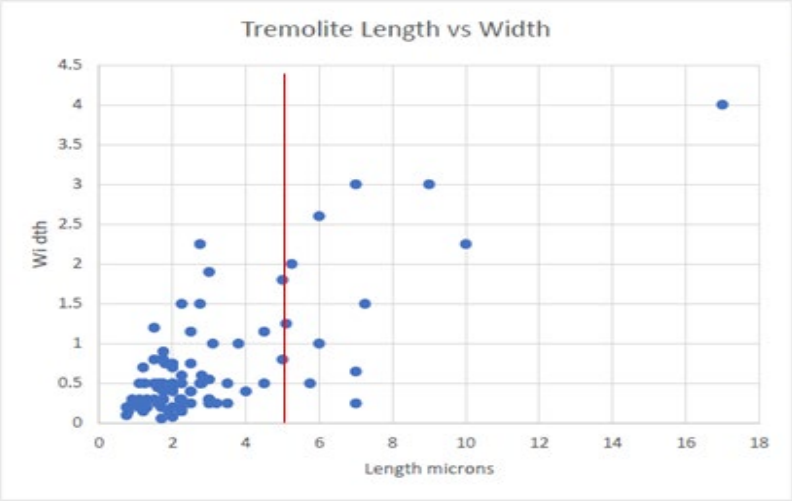


Figure F-2. Detection of tremolite by TEM in a cosmetic product that was "not detected" by PLM. As shown, most tremolite particles identified by TEM in this sample population were < 5 um in length and < 1 um in width.

3. Issues in the Identification and Classification of Mineral Particles

A. Mineral Identification

Confirmation of the mineral identity of each particle requires a determination of its elemental composition and crystal structure. PLM, used with dispersion staining, can provide a preliminary assessment of the identities of mineral particles by differences in their optical properties. TEM methods can distinguish differences in both elemental composition and crystal structure. TEM coupled with EDS provides information about the elemental composition of the mineral particle. TEM coupled with SAED provides information about the crystal structure of individual particles. Thus, compared with PLM, TEM/EDS and TEM/SAED better enables the analyst to confirm mineral identity.

In asbestos testing of talc and talc-containing cosmetic products, the most common mineral particles are chrysotile, the amphibole minerals tremolite, actinolite and anthophyllite, and to a lesser extent amphibole/talc intergrowths. The individual fibers and fibrils of the mineral chrysotile manifest a unique scrolled hollow structure. Thus, identification of chrysotile using TEM/SAED and TEM/EDS is relatively straightforward. By contrast, due to myriad possibilities for elemental substitution (e.g., Na, K, Ca, Fe(II)) in amphibole crystals there are many known and possible amphibole mineral compositions. Fortunately, the naming conventions for amphiboles in geology references allow for some degree of variation in elemental substitution at positions in the double chain silicate crystal. Whenever the mineral type is ambiguous laboratories may want to consider using the general term "amphibole." Although talc and

anthophyllite have similar elemental composition and crystal structures, differentiation between talc and anthophyllite is possible when the particles are viewed from at least two angles (i.e., dual zone axis SAED patterns are obtained).[23]

Currently, while SEM/EDS provides comparable elemental composition as TEM/EDS, SEM is inferior to TEM at providing the analyst with the necessary information on crystal structure to make a definitive mineral identification (**Figure F-3)**. Recent advances in EBSD cameras, with field emission SEM are showing some promise toward improving capability of SEM for mineral identification.

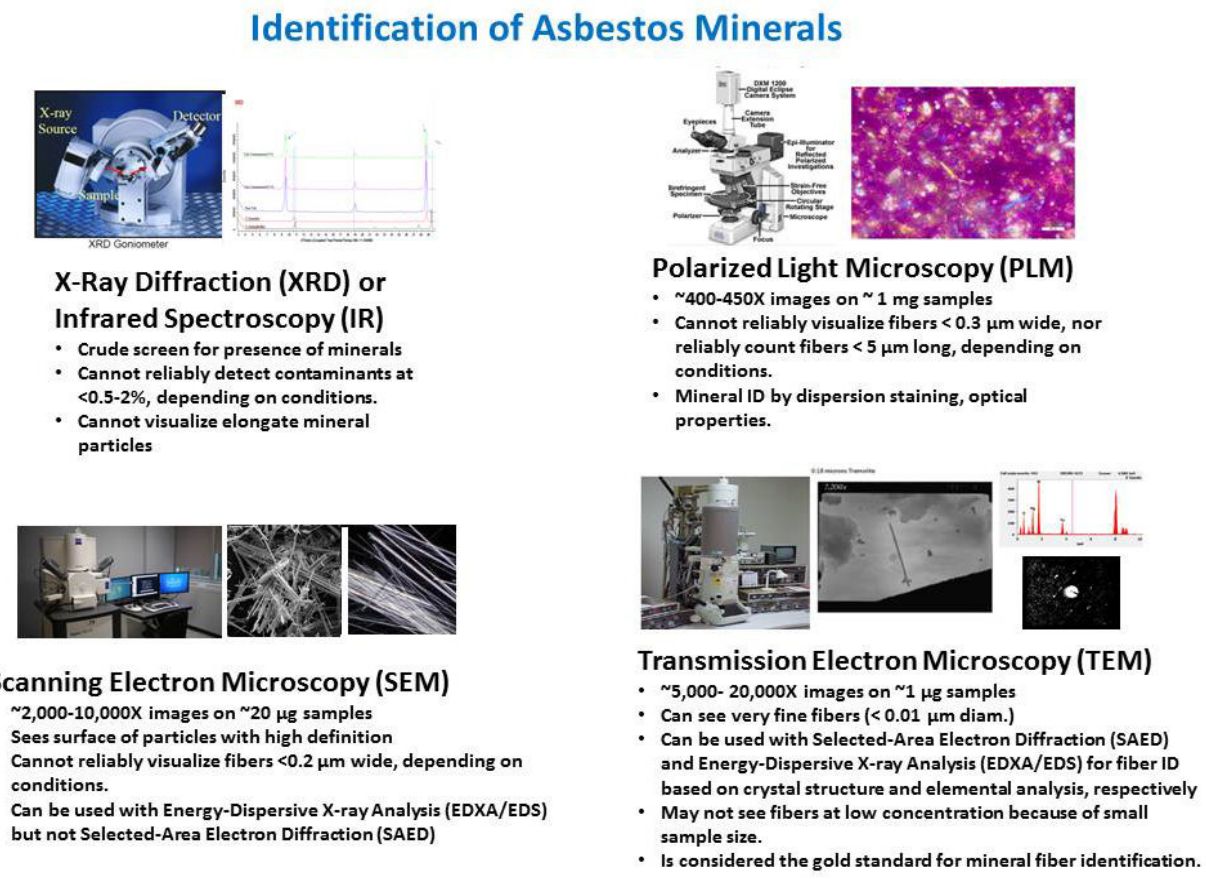


Figure F-3. Commonly Used Methods for the Detection and Identification of Asbestos Minerals in Talc. Each method has different limitations, and optimally, analysts use a combination of most or all of these methods. Photos: J. Januch and miscellaneous government sources.

[23] M. Gunter presentation at February 4, 2020 Public Meeting, see https://www.fda.gov/media/135066/download.

B. Classification of Habit of Growth of Mineral Particles Based on Morphology

The term "asbestiform" implies a unique fibrous habit of growth and related properties that are commercially important. Particularly when using TEM, the analyst may be unable to determine the growth habit of amphibole particles dispersed at low concentration in milled talc or a cosmetic. (See below as well as ***Appendix D*** for additional explanation.)

Consideration A: Particle Dimensions

Asbestos and other amphibole particles found in nature exhibit a range of particle lengths, widths, and aspect ratios. Thus, when populations of amphibole or chrysotile particles in a sample of talc or a talc-containing cosmetic are measured, there is a likelihood of finding a broad distribution among particle dimensions of length and width as well as the respective calculated aspect ratios. Some researchers have suggested that populations of amphibole asbestos fibers can be differentiated from non-asbestiform particles or cleavage fragments based on population width distributions reflecting differing tendencies in particle attrition among the two growth habits (Blount, 1991; Van Orden et al. 2008, 2009; Harper et al. 2008). General guidelines for differentiation based on dimensions do not exist, although there are minima for length and aspect ratio for asbestos counting in published standards. The strict application of length and aspect ratio as measures to differentiate asbestiform and non-asbestiform particles remains debated in the scientific literature. Thus, IWGACP is not in favor of using dimensional criteria to differentiate asbestiform and non-asbestiform particles in talc and cosmetics.

Consideration B: Particle Shape

The attempts to characterize mineral particle habit of growth (asbestiform or non-asbestiform) based on particle shape has long been the subject of disputes between asbestos-testing laboratories. Differentiation between asbestiform and non-asbestiform particles of an amphibole mineral often hinges on subjective interpretation of a mineral particle's observed fine structure (Aust et al. 2011; ***Appendix D***). Even if there are differences in potency between asbestiform and non-asbestiform particles in terms of health effects, which is still debatable, it is difficult to discern asbestiform and non-asbestiform particles.

Using TEM, the distinguishing feature exhibited by fibers and fibrils of chrysotile due to the scrolling of this sheet silicate mineral are unmistakable, provided the fiber has not been degraded by extensive exposure to the electron microscope beam. In marked contrast, the individual fibers of asbestiform amphiboles lack any such distinguishing characteristic. Bundles of asbestiform amphibole can be reduced in size, and hence are less likely to be present after extensive processing, such as from the milling of talc to produce cosmetics. As a result, there have been disputes between laboratories over whether amphibole particles detected by TEM are to be regarded as "asbestos," or rather as having arisen from attrition and/or fracture of larger particles

of a non-asbestiform analog. The EPA's regulations promulgated under AHERA and ISO 10312:2019 standards for TEM analysis of asbestos fibers offer figures depicting a variety of asbestiform amphibole structures, including single fibers as well as complex structures consisting of fibers (***Appendix F***). As noted in the Scope section of the ISO 10312:2019 standard, TEM methods cannot readily discriminate between individual fibers of asbestos and non-asbestos analogues of the same amphibole mineral. **Figure F-4** illustrates particles of tremolite that have stepped ends and could be regarded as being asbestiform applying the definitions of asbestos in the ISO standard.

The definition of asbestos in the Talc USP standard, "*parallel fibers occurring in bundles, fiber bundles displaying frayed ends, fibers in the form of thin needles, and matted masses of individual fibers and/or fibers showing curvature*," is based on the appearance characteristic of bulk asbestos and is only applicable to PLM. As suggested in the narratives of the EPA Method for Determination of Asbestos in Bulk Materials (EPA 600/R-93/116) and the OSHA Method for Bulk Materials (ID-191), the characteristics of bulk asbestos should only be used for identification of asbestiform structures detected in the analysis of bulk materials by PLM.

Conceivably, a sample to be tested for asbestos can contain a mixture of asbestiform and non-asbestiform amphiboles. ***Appendix D*** shows electron microscope images of amphibole samples collected in areas where there had been commercial vermiculite and talc mining, respectively, indicating the diverse morphology of amphiboles that can exist within a single mine or across a region. These images further demonstrate that even when the sample provenance is known, it is difficult to classify the growth habit of an amphibole particle as either asbestiform or non-asbestiform from electron microscope images at high magnification.

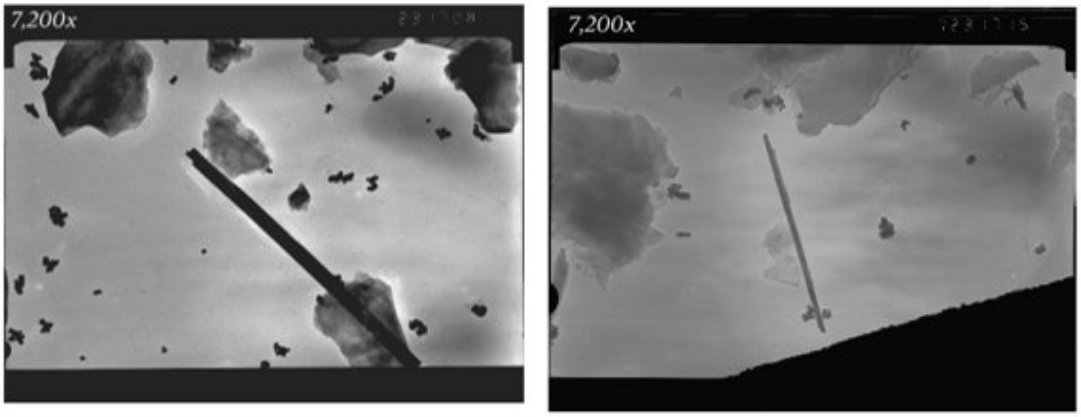


Figure F-4. Appearance of Asbestos vs. Non-asbestiform Mineral Particles. Both images are tremolite mineral particles narrower than about 0.5 µm that have essentially parallel sides and may be stepped at their ends. Lacking the bundled appearance of bulk asbestos, it may be unclear whether these mineral particles were derived from dissociation of tremolite asbestos or tremolite that crystallized in a non-asbestiform habit. As a result, different laboratories might arrive at different conclusions regarding whether or not these mineral particles should be characterized as "tremolite asbestos." Images are taken from an AMA laboratory report posted on an FDA website https://www.fda.gov/media/122414/download.

To account for and describe the morphology of amphibole particles detected, IWGACP advises applying the definitions for the types of particle structures in standards for TEM: ISO 10312:2019 (Annex C sections C.2.1 through C.2.5),[24] and ISO 13794:2019 (Annex D sections D.2.1 through D.2.5), rather than attempting classification based on dimensions or shape. These sections of the ISO standards provide relevant terminology and exemplary pictorial representations for amphibole particles detected in talc and talc-containing cosmetics by TEM. Representative images such as those in **Figure F-4**, typifying the morphologies exhibited by the population of amphibole particles detected in samples of talc and talc-containing cosmetics, should also be provided in the laboratory report.

A more detailed discussion of amphibole morphology and crystal habit and the associated issues in characterization of asbestiform, fibrous, and other habits of amphibole can be found in Meeker, et al 2003 and ***Appendix D***.

C. Types of Asbestiform and Other Mineral Particle Structures Observed Using TEM

Figures F-5 and **F-6** depict Asbestos Fiber Structures, and Particle Morphologies, respectively. Single fibers, bundles, clusters and matrices are termed "primary structures." Fibers in contact with other particles i.e., in bundles, clusters and matrices (i.e., "secondary structures"), may be counted individually or as collectively as part of a primary structure. The methods for quantitation of structures and/or fibers can be specified in a regulation or regulatory method.

[24] As stated in structure definitions, "Each fibrous structure that is a separate entity shall be designated as a primary structure. Each primary structure shall be designated as a fibre, bundle, cluster or matrix...." (ISO 10312 2019).

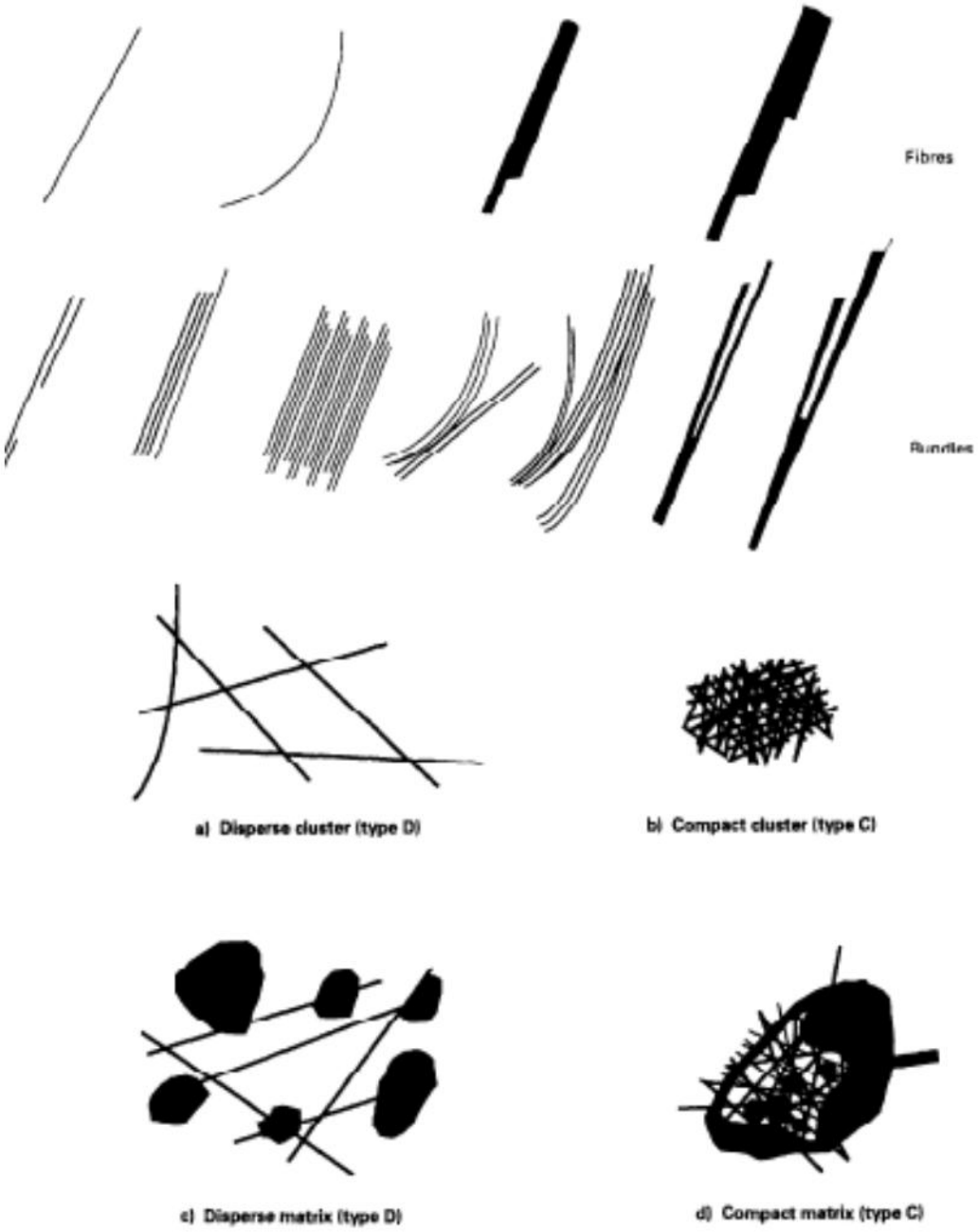


Figure C.1 — Fundamental morphological structure types

Figure F-5. Asbestos Fiber Structures. Source: ISO 10312 (2019) for analysis of asbestos on filters used to collect air samples (the same figure also appears in ISO 13794 [2019]); ©ISO. This material is adapted from ISO 10312:2019, with permission of the American National Standards Institute (ANSI) on behalf of the International Organization for Standardization on 8/6//20 via email to S. Wolfgang. All rights reserved.

Figure F-6. Particle Morphologies. Source: Modified from Campbell et al. (1977) page 24.

4. Issues Related to Quantitative Analysis/Counting of Asbestos and Other Amphibole Mineral Particles.

PLM has limitations as either a qualitative or quantitative method for asbestos in talc and cosmetics. PLM instructions for quantifying asbestos were developed for the purpose of risk management (assessment and mitigation), cognizant of the limitation in light microscopy resolution and mindful of the desire to ensure reproducibility when quantifying asbestos. Therefore, protocols for light microscopy typically exclude the reporting of short particles (<5 µm in length) and/or structures approximately 0.2 µm or less in width, and thus, tend to exclude many of the particles of interest. This can lead to underreporting or false negative findings, especially when testing a talc-containing cosmetic product that has been milled and processed. IWGACP concluded that the most inclusive dimensional criteria from instructions for quantifying asbestos test methods should be applied to avoid underreporting of the amount present or false negative findings when testing a talc-containing cosmetic product.

Qualitative Analysis. PLM and TEM are complementary methods for the qualitative analysis (detection) of asbestos and other amphibole mineral particles in talc. PLM can detect larger amphibole and chrysotile particles, e.g., bundles of asbestos, while TEM can detect particles too narrow to be detected using a light microscope (0.2-0.4 µm width), including chrysotile fibers and amphiboles that are not in the form of bundles, hence less readily characterized as to the nature of their growth habit.

Quantitative Analysis. PLM and TEM are also capable of quantitation of asbestos and other mineral particles, however accurate quantitation poses challenges, and can lead to inaccurate values that may be difficult to interpret. Quantitation in a bulk sample may involve determination based on weight percent (most commonly used to count asbestos by PLM) or based on a count of the number of fibers (most commonly used to count asbestos by TEM) detected. Quantitation by PLM and more so, by TEM, relies on extrapolation of amounts detected in very small amounts of sample and fields of view to much larger amounts of talc or talc-containing product. Moreover, quantitative analysis is expected to be less reproducible when the percentage of the mineral of interest in the bulk material is well below 1% by weight or when the fiber counts are relatively small.

Thus, accurate quantitation by TEM, particularly as a weight percent, poses various challenges associated with sample size relative to the product. For example, the presence of a single relatively wide particle in the detected particle population could skew the mass of particles and indicate the weight percent to be much higher than it would be had a larger amount of sample been analyzed. By contrast, narrower particles contribute relatively little to the total mass yet could be considered more hazardous than wider particles on a per gram basis. Importantly, for a given mineral type or classification (e.g., chrysotile), the number of particles in the substance seems likely to be more indicative of a potential health hazard than the collective particle mass.

For cosmetics, it appears that any given type of mineral particle in the sample at a relatively low level will not necessarily be homogeneously distributed and that the number of visualized particles will tend to be small. IWGACP review of laboratory reports for talc-containing cosmetics indicates that, historically, confidence limits have not been provided to account for uncertainties in sampling and measurement of asbestos and other mineral particles. Issues with sampling are discussed briefly in ***Appendix I***.

In conclusion, all of these factors raise concerns that quantitation of asbestos and other amphibole mineral particles from a single test result can be inaccurate and imprecise.

5. Asbestos Fiber Counting Criteria in Published Test Methods

Group	Protocol	Year	Instrumental Method	Matrix	Resolution: Min Width Detectable [1]	Min Fiber Length	Max Fiber Length	Min Fiber Width	Max Fiber Width	Min Aspect Ratio	Fiber morphology	Brief Description and Limitations of Protocol
Bulk Materials such as Talc/Soil	**CTFA J4-1**[2]	1976	PLM (if XRD is positive)	Talc	0.2-0.3 µm	NA	30 µm		3 µm	5:1		Method to determine asbestiform amphibole minerals in cosmetic talc. This method cannot rule out presence of amphibole asbestos at less than 0.5%. Uses X-ray diffraction (XRD) to screen for amphibole. Method is not designed to report serpentine or chrysotile and likely will not detect serpentine if due to chrysotile in talc especially if chlorite, which interferes, is present. If XRD is positive, then polarized light microscopy (PLM) must be used to look for amphibole asbestos fibers. PLM cannot resolve fibers < 0.2 µm in width nor reliably detect fibers < 5 µm long.
Bulk Materials such as Talc/Soil	**USP Talc Monograph**[3]	2013	PLM (if IR or XRD is positive)	Talc	0.2-0.3 µm	5 µm.			NA	20:1	Asbestiform as indicated by 2 or more of the following: 1) parallel fibers occurring in bundles, 2) fiber bundles displaying frayed ends, 3) fibers in the form of thin needles, 4) matted masses of individual fibers and/or fibers showing curvature.	Method to determine asbestiform amphibole minerals and chrysotile in pharmaceutical talc applies similar XRD screening approach with similar limitations as described above for CTFA J4-1. (Also allows optional use of IR to screen for amphibole or serpentine, but this option is expected to be eliminated in a future revision to the monograph.) With respect to the XRD/PLM methodology, provides reference to USP general chapter <941>: X-RAY DIFFRACTION microscopy method and USP general chapter <776>: OPTICAL MICROSCOPY. Both

Group	Protocol	Year	Instrumental Method	Matrix	Resolution: Min Width Detectable [1]	Min Fiber Length	Max Fiber Length	Min Fiber Width	Max Fiber Width	Min Aspect Ratio	Fiber morphology	Brief Description and Limitations of Protocol
												general chapters lack information for optimizing sensitivity and specificity of the overall analysis, leading to significant potential for false negatives and/or mischaracterization of the minerals.
Bulk Materials such as Talc/Soil	**EPA-600/R-93/116[4]**	1993	PLM	Bulk Building materials	0.2-0.3 µm	5 µm avg.			0.5 µm avg.	20:1 avg.	Asbestiform	Measurement of asbestos in solid samples (vermiculite, building materials, soil, etc.) usually is performed by PLM, which uses the optical properties of asbestos to identify and classify different types of asbestos fibers. In general, these methods are most reliable for materials that contain relatively high concentrations of asbestos, and results tend to become more variable as concentrations decrease below about 1% by mass. In this protocol, only those fibers with "asbestiform" features are counted.
Bulk Materials such as Talc/Soil	**ASTM D7521-16[5]**	2016	PLM (optional, TEM)	Soil	0.2-0.3 µm for PLM	0.5 µm			NA	5:1	Substantially parallel sides	Method for determination of asbestos in soil by PLM and optional for TEM with SAED and EDS, including methods for gravimetric, sieve, and other sample preparation procedures. Has an analytical sensitivity of 0.25% by weight, with optional procedures (TEM) to achieve 0.1% sensitivity.
Bulk Materials such as Talc/Soil	**OSHA ID-191[6]**	1992 rev. 1995	PCM/PLM	Bulk materials ; can include talc.	0.2-0.3 µm for PCM and PLM	5 µm				3:1	Long, bundled appearance	OSHA method for gross examination, phase-polar microscopy, and central stop microscopy PCM/PLM of asbestos in bulk samples. Detection limit is less than 1% by area. Although good for a quick look at a larger sample

Group	Protocol	Year	Instrumental Method	Matrix	Resolution: Min Width Detectable [1]	Min Fiber Length	Max Fiber Length	Min Fiber Width	Max Fiber Width	Min Aspect Ratio	Fiber morphology	Brief Description and Limitations of Protocol
												(than would be used for EM), PCM cannot reliably detect short fibers (< 5 µm) nor resolve thin fibers (<~0.2 µm). Precision and accuracy are analyst-dependent.
Dust/Wipe Samples	**ASTM D5755-09e1**[7]	2014	TEM [8]	Dust	0.03 µm	0.5 µm			NA	5:1	Substantially parallel sides	Method for microvacuum sampling and indirect analysis of non-airborne dust by TEM at 15,000-20,000X with SAED and EDS for asbestos structure loading starting at 1,000 asbestos structures/cm^2. (Collection efficiency is unknown and will vary between substrates.) A companion method, ASTM D5756 is the same except it uses a direct approach.
Dust/Wipe Samples	**ASTM D6480-19**[9]	1999, rev. 2010	TEM	Dust	0.03 µm	0.5 µm			NA	5:1	Parallel or stepped sides	Method for wipe-testing of surfaces, indirect preparation, and analysis for asbestos structure number surface loading by TEM with SAED and EDS. It is intended to disperse asbestos aggregates and, like all indirect sample prep techniques, may not represent the physical form of the asbestos as sampled. It cannot always discriminate between individual fibers of the asbestos and non-asbestos analogues of the same amphibole mineral. Collection efficiency will vary among substrates. Because microscopists have varied in their ability to detect very small asbestos fibers, a minimum length of 0.5 µm was defined in the method as the shortest fiber to be incorporated in the results report.

Group	Protocol	Year	Instrumental Method	Matrix	Resolution: Min Width Detectable [1]	Min Fiber Length	Max Fiber Length	Min Fiber Width	Max Fiber Width	Min Aspect Ratio	Fiber morphology	Brief Description and Limitations of Protocol
Air Samples	**NIOSH 7400**[10]	1989 rev. 1994	PCM	Air	0.2-0.3 µm	5 µm	100 µm		NA	3:1	NA	Method for measuring asbestos (fibers/cc) in air samples collected on filters. PCM identifies countable fibers based only on morphology and does not consider mineralogy or crystal structure. PCM cannot classify asbestos fibers by mineral type or differentiate asbestos and non-asbestos fibers. Fibers that cross the graticule boundary more than once are not counted.
Air Samples	**OSHA ID-160**[11]	1988 rev. 1997	PCM	Air	0.2-0.3 µm	5 µm			NA	3:1	NA	Another method for measuring asbestos fibers in air samples collected on filters. Detection limit is 0.001 fibers/cc in 2400 L of air. PCM (at 400X), again, does not positively identify asbestos fibers, and cannot detect fibers < 0.2 µm in diameter, whereas fine asbestos fibers may be smaller.
Air Samples	**ASTM D7200-12**[12]	2006 rev. 2012	PCM TEM	Air	0.2 µm for PLM; 0.03 µm for TEM	5 µm			3.0 µm	3:1	Asbestiform habit	Method to determine asbestos fibers/mL of air collected on filters, based on methods ISO 8672, NIOSH 7400, and OSHA ID 160. Ideally, counts 100- 1300 fibers/mm^2 of filter area, or 0.04 to 0.5 fibers/mL for 1000L of air sampled. The TEM is used for assistance in identification of fibers.
Air Samples	**ASTM D7201-20**[13]	2006 rev. 2011, rev. 2020	PCM (optional TEM)	Air	0.2-0.3 µm for PLM (optional 0.03 µm for TEM)	5 µm			3.0 µm	3:1	Asbestiform habit	Method for sampling and counting airborne asbestos by PCM, with optional TEM- ideally 100-1300 fibers/mm^2 of filter, corresponding to 0.04-0.5 fibers/mL from a 1000 L air sample; LOD 0.0027 fiber/mL.

Group	Protocol	Year	Instrumental Method	Matrix	Resolution: Min Width Detectable [1]	Min Fiber Length	Max Fiber Length	Min Fiber Width	Max Fiber Width	Min Aspect Ratio	Fiber morphology	Brief Description and Limitations of Protocol
Air Samples	**NIOSH 7402**[14]	1989 rev. 1994	TEM	Air	0.03 µm	5 µm		0.25 µm	NA	3:1		Uses the TEM with EDS and SAED for analysis of asbestos in air samples. This method is a compliment to the NIOSH 7400 method in that it uses qualitative methods (morphology, chemical composition by EDS, and electron diffraction by a comparison method) to verify fiber counts and identify fibers as asbestos, or not, from a NIOSH 7400 PCM optical analysis. NIOSH 7402 requires SAED analysis of a minimum of 10% of the fibers, and at least 3 asbestos fibers, by EDS and SAED to confirm the presence of asbestos. Fiber counts are done at the same magnifications as NIOSH 7400 (500-1000x) with fiber dimensions being measured at 10,000x.
Air Samples	**EPA AHERA**[15]	1987	TEM	Air	0.03 µm	0.5 µm			NA	5:1	Substantially parallel sides	Method for determination of remaining friable asbestos in air after asbestos abatement in schools. TEM grids are assessed at 250-1,000X, then analyzed at 15,000-20,000X. The number of 200 mesh electron microscope grid openings counted is adjusted to achieve a sensitivity of 0.005 structures/cc based on volume and effective filter area.
Air Samples	**ISO 10312**[16]	2019	TEM	Air	0.03 µm	0.5 µm fibers 5 µm asbestos			NA	5:1 3:1	Parallel or stepped sides	Direct transfer TEM (with SAED, and EDS) method for determination of asbestos fibers in ambient air. ISO 10312 defines a fiber as an elongated particle with parallel or stepped sides, an aspect ratio of 5:1, and a minimum length of 0.5 µm.

Group	Protocol	Year	Instrumental Method	Matrix	Resolution: Min Width Detectable [1]	Min Fiber Length	Max Fiber Length	Min Fiber Width	Max Fiber Width	Min Aspect Ratio	Fiber morphology	Brief Description and Limitations of Protocol
												Alternatively, the detected particles may be expressed as PCM-equivalent fibers (PCMe), defined as those structures having an aspect ratio greater than or equal to 3:1, longer than 5 µm, and a diameter between 0.2 µm and 3.0 µm. As stated in the Scope section, "this method cannot discriminate between individual fibres of the asbestos and elongate fragments (cleavage fragments and acicular particles) from non-asbestos analogues of the same amphibole mineral". However, the standard provides an Annex showing examples of the shapes and configurations of various types of asbestiform structures. ©ISO. This material is adapted from ISO 10312:2019, with permission of the American National Standards Institute (ANSI) on behalf of the International Organization for Standardization on 8/6/20 via email to S. Wolfgang. All rights reserved.
Air Samples	**ISO 13794**[17]	2019	TEM	Air	0.03 µm	0.5 µm			NA	5:1	Parallel or stepped sides	Indirect transfer TEM (with SAED, and EDS) method for determination of asbestos fibers in ambient air. See ISO 10312 for additional information. ©ISO. This material is adapted from ISO 13794:2019, with permission of the American National Standards Institute (ANSI) on behalf of the International Organization for Standardization on 8/6/20 via email to S. Wolfgang. All rights reserved.

Group	Protocol	Year	Instrumental Method	Matrix	Resolution: Min Width Detectable [1]	Min Fiber Length	Max Fiber Length	Min Fiber Width	Max Fiber Width	Min Aspect Ratio	Fiber morphology	Brief Description and Limitations of Protocol
Air Samples	**ASTM D6281-15**[18]	1998, rev. 2009, rev. 2015	TEM	Air	0.03 µm	0.5 µm			NA	5:1	Parallel or stepped sides	Method developed for determination of airborne asbestos concentration in ambient and indoor atmospheres by collection on filters and direct transfer to TEM grids followed by TEM analysis. TEMs typically have sub-micrometer limit of resolution, however, because microscopists have variations in their ability to detect very small asbestos fibers, a minimum length of 0.5 µm was defined as the shortest fiber to be reported in the results.
Water Samples	**EPA 100.1**[19]	1983	TEM	Water	0.03 µm	0.5 µm			NA	3:1	Parallel or stepped sides	Method for determination of asbestos fibers in water; like air methods, based on filtration. Filters are examined by TEM at 20,000X with SAED (for crystal structure) and EDS (for elemental composition).
Water Samples	**EPA 100.2**[20]	1994	TEM	Water	0.03 µm	10 µm			NA	3:1	Substantially parallel sides	Method for determination of asbestos structures >10 µm in length in drinking water based on morphology (TEM at 20,000-25,000X), crystal structure (SAED) and elemental analysis (EDS).

[1]Inferred from method used and may not necessarily be stated in the source document; inferred limit is based on limit of resolution of light microscopy methods (0.2-0.3 µm).
[2]https://www.cir-safety.org/sites/default/files/032013_web_w2.pdf ; starting at page 73
[3] Printed on: Wed Jan 22, 2020, from: https://online.uspnf.com/uspnf/document/GUID-DBC75D3B-0CA7-4F0D-9019-4F96B6BE454B_1_en-US, © 2020 USPC.
[4]Available from https://nepis.epa.gov.
[5]Available through www.astm.org at https://www.astm.org/Standards/D7521.htm.
[6]Available at https://www.osha.gov/dts/sltc/methods/inorganic/id191/id191.html.
[7]Available through www.astm.org at https://www.astm.org/Standards/D5755.htm.

[8]The theoretical and practical minimum resolution of a TEM is orders of magnitude less than that of visible light-based microscopes and in many cases sub-micrometer. The TEM resolution depends on many factors in the microscope [*e.g.* electron energy; electron beam characteristics (lenses, apertures, etc.); detector; etc.]. Any reporting of minimal length or width of structures is based on text in the method.
[9]Available through www.astm.org at https://www.astm.org/Standards/D6480.htm.
[10]Available at https://www.cdc.gov/niosh/nmam/pdf/7400.pdf
[11]Available at https://www.osha.gov/dts/sltc/methods/inorganic/id160/id160.html
[12]Available through www.astm.org at https://www.astm.org/Standards/D7200.htm.
[13]Available through www.astm.org at https://www.astm.org/Standards/D7201.htm.
[14]Available at https://www.cdc.gov/niosh/docs/2003-154/pdfs/7402.pdf.
[15]Available at https://www.govinfo.gov/content/pkg/CFR-2011-title40-vol31/pdf/CFR-2011-title40-vol31-part763-subpartE.pdf.
[16]Available through www.iso.org at https://www.iso.org/obp/ui/#iso:std:iso:10312:ed-2:v1:en.
[17]Available through www.iso.org at https://www.iso.org/standard/75576.html.
[18]Available through www.astm.org at https://www.astm.org/Standards/D6281.htm.
[19]Also known as EPA/600/4-80-005, EPA/600/4-83-043 and EPA-NERL 100.1; available through www.nemi.gov at https://www.nemi.gov/methods/method_summary/5757/.
[20]Also known as EPA/600/R-94/134 and EPA-NERL 100.2; available through www.nemi.gov at https://www.nemi.gov/methods/method_summary/5758/.

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APPENDIX G: LAWS, REGULATIONS, AND ACTIONS BY FEDERAL AGENCIES PERTAINING TO ASBESTOS

Various federal agencies have jurisdiction over asbestos or the asbestos content of talc at various stages of the mining and manufacturing processes. The Mine Safety and Health Administration (MSHA) is dedicated specifically to protecting miners, including talc miners, in the U.S. The Occupational Safety and Health Administration (OSHA) is charged with ensuring worker safety, including that of US workers who use talc during product manufacturing. FDA has regulatory authority over cosmetics, foods (including dietary supplements), and medical products (including drugs and devices) which can contain talc. The Consumer Product Safety Commission (CPSC) has authority over consumer products other than those regulated by the FDA and other federal agencies. Environmental and non-occupational hazards related to asbestos fall under the purview of the U.S. Environmental Protection Agency (EPA).

Table G-1 lists U.S. laws, regulations, and actions by federal agencies regarding asbestos. There are variations in the statutory mandates and regulatory standards of measurements, testing methods, identification and quantitation written by the various federal agencies with regard to how "asbestos" is defined. This variation, in part, derives from the differences in the situations each agency regulates, differences in the sample matrices subject to testing (e.g., air, water, soil, bulk samples, building materials, or processed consumer products), varying needs for sensitivity and specificity, an evolving understanding of what information is necessary to address health concerns in various situations, and the influence of non-government stakeholders.

Standards vary in terms of counting particles with respect to specified particle length, particle width, and particle aspect ratio criteria, as well as which nominal dimensions are practical limits given the limitations of the methods prescribed (***Appendix F.5***). However, specific dimensions have typically been chosen as a matter of convenience or based on limitations in analytical sensitivity at the time, rather than on a firm understanding of the potency of different fiber types and sizes with respect to risk of human disease. For example, the USP talc monograph used in FDA drug specifications currently counts only particles ≥ 5 µm in length, (given instrument resolution, minimum width is effectively 0.2-0.4 µm), and > 20:1 in aspect ratio. By contrast, the test method in EPA's regulations promulgated under AHERA[25] to protect students and school employees from exposure to airborne asbestos in school buildings, uses a more sensitive microscope (TEM) and more expansive instructions for quantification of asbestos which allow

[25] 40 CFR Part 763.

the counting of particles ≥ 0.5 µm length, (effectively <0.03 µm in width), and 5:1 in aspect ratio, irrespective of morphology. The minimum particle length of 5 µm cited in many protocols is not derived from health data, but rather is the lower limit of what could be observed reliably using light microscopy.

Exposure limits for asbestos vary by agency. MSHA and OSHA, for example, set permissible occupational exposure limits for workers who generally know to what they may be exposed and have some idea of the risk and risk mitigation strategies. On the other hand, the FDA considers the presence of asbestos in a talc-containing cosmetic product to adulterate this product because it may render the product injurious to users under the conditions of use.

Table G-1 U.S. laws, regulations, and actions by federal agencies regarding asbestos.

U.S. Agency/Division	Laws, regulations, or relevant actions
Food and Drug Administration (FDA)	Any product regulated by FDA (including cosmetics, foods, drugs, and devices) that contains asbestos may be deemed adulterated in accordance with the relevant FDA statutory provisions.
Consumer Product Safety Commission (CPSC)	CPSC regulates the risks posed by more than 15,000 consumer products, including some containing asbestos as a known ingredient and others that have contained asbestos as a contaminant. In 16 CFR § 1304.3 and 16 CFR § 1305.3, CPSC defined asbestos as "a group of mineral fibers composed of hydrated silicates, oxygen, hydrogen and other elements such as sodium, iron, magnesium and calcium in diverse combinations," which include "amosite, chrysotile, crocidolite, anthophyllite asbestos, actinolite asbestos, and tremolite asbestos."
Consumer patching compounds; artificial emberizing materials (ash and embers)	In 1977, CPSC banned asbestos-containing consumer patching compounds and artificial fireplace ash and embers, citing risk of lung cancer or mesothelioma upon respiration (16 CFR 1304, 16 CFR 1305). Patching compounds, such as drywall spackling compounds and tape joint compounds available in dry form or as pastes, were mixtures of talc, pigments, clays, casein, ground marble, mica, or similar materials that contained intentionally added asbestos. Emberizing materials were found to contain up to 50% asbestos.
Hair dryers	In 1979-1980, CPSC announced agreements with hair dryer manufacturers, and conducted several recalls of hair dryers manufactured with asbestos (e.g., https://www.cpsc.gov/Recalls/1979/cpsc-accepts-corrective-actions-from-major-hair-dryer-companies).
Crayons/Chalk	In 2000, CPSC evaluated crayons reported to contain asbestos. https://www.cpsc.gov/s3fs-public/pdfs/crayons.pdf. Three firms agreed to reformulate. CPSC found no asbestos in children's chalk. https://www.cpsc.gov/content/cpsc-testing-finds-no-asbestos-fibers-in-childrens-chalk.
Environmental Protection Agency (EPA)	EPA has multiple laws and regulations addressing asbestos. For more information, see https://www.epa.gov/asbestos/asbestos-laws-and-regulations

U.S. Agency/Division	Laws, regulations, or relevant actions
Occupational Safety and Health Administration (OSHA), Mine Safety and Health Administration (MSHA)	OSHA and MSHA regulate asbestos exposures in occupational settings (MSHA regulations specifically apply to miners and millers of ores). Asbestos mining is no longer permitted in the U.S., but current miners could be exposed to asbestos that is associated with talc, vermiculite, taconite, gold, and other ores. OSHA regulates mineral dust exposures to general industry workers under 29 CFR 1910 and to construction workers under 29 CFR 1926. OSHA defines asbestos as the six regulated mineral fibers (the serpentine mineral chrysotile, and the amphibole minerals cummingtonite-grunerite asbestos (amosite), riebeckite asbestos (crocidolite), actinolite asbestos, anthophyllite asbestos, and tremolite asbestos) (29CFR 1910.1001(b)). OSHA's current permissible exposure limit (PEL) for asbestos (collectively, all 6 types) is 0.1 fibers/cm^3 for an 8-hour time weighted average (TWA) exposure (59 FR 40964-41162). For determining compliance with the PEL, OSHA regulations define asbestos fibers as any of the 6 minerals occurring in the "asbestiform growth habit" having length $\geq$ 5 µm and aspect ratio $\geq$3:1 as observed under a 400x PLM. Testing is by the OSHA ID-160 and NIOSH 7400 methods. OSHA's PEL for "talc not containing asbestos" was set in 1972, and remains at 20 million particles per cubic foot of air (mppcf) (58 CFR 35338, June 30, 1993). Talc containing asbestos is subject to the PEL for asbestos. Currently, under OSHA guidelines, fibrous talc and tremolite that is claimed to be non-asbestiform are subject to the PEL for "particles not otherwise regulated" (PNOR): 5 mg/m^3 for respirable dust and 15 mg/m^3 for total dust (57 FR 24310; June 8, 1992). The MSHA asbestos PEL for miners is 0.1 fibers/cc over 8 hours (defined similarly to OSHA), and the allowable limit for brief exposures to higher asbestos levels is 1 fiber/cc over a 30- minute period (73 FR 11283). MSHA defines "*fibrous talc*" as "a magnesium silicate ($Mg_3Si_4O_{10}(OH)_2$) $\geq$ 5 µm and AR $\geq$3:1. Fibrous talc has the same fiber limit as asbestos. This is due to the similarity of the reaction in the lungs produced by fibrous talc and asbestos fibers (https://arlweb.msha.gov/S&HINFO/OPRSAMP/OPRSAMP.HTM).
Other agencies: National Institute for Occupational Safety and Health (NIOSH), Agency for Toxic Substances and Disease Registry (ATSDR), National Institutes of Health (NIH), US Geological Survey (USGS), National Institute of Standards and Technology (NIST)	While some other federal agencies have no regulatory mandate, they have important expertise relevant to this discussion. The NIOSH is engaged in scientific research related to occupational health in support of OSHA's mission. The ATSDR supports the public health by preventing harmful exposures. The NIH and USGS are U.S. agencies dedicated to medical and geological research, respectively. NIST operates an accreditation program for laboratory technicians engaged in asbestos-testing.

APPENDIX H: LABORATORY QUALIFICATIONS

This section contains the outcome of the deliberations among scientific experts in the IWGACP regarding qualification programs that have been developed to enable laboratories to demonstrate proficiency in asbestos analysis. In this section, IWGACP discusses some key aspects for performing reliable analyses and qualification programs for FDA's consideration. These scientific opinions and related advice do not represent recommendations or policies of the FDA or any other federal agency.

The IWGACP advises that, given the complexities of asbestos analysis, laboratories should have adequately trained analysts with demonstrated proficiency in mineral analysis and in the methods used to analyze samples of talc and talc-containing cosmetics. The IWGACP recognizes that formal training in mineral identification, use of quality management systems (e.g., ISO 10012; ISO 17025), use of established (published) methods, and participation in proficiency testing using well-characterized materials are beneficial toward ensuring the reliability of the asbestos analysis.

1. Qualifications of a Laboratory for Detecting Asbestos in Talc

In response to the February 4, 2020 Public Meeting on Testing Methods for Asbestos in Talc and Cosmetic Products Containing Talc a docket[26] contained comments suggesting that insufficient analyst education in mineralogy may lead to inaccurate reports of asbestos due to mischaracterization of minerals. The IWGACP agrees that certain qualifications are necessary and that only competent individuals trained in mineral detection and identification should be conducting analysis of talc and cosmetics for asbestos minerals. However, the IWGACP concludes that an advanced degree in mineralogy is not a prerequisite for individuals conducting asbestos analysis routinely in commercial, industry, or government laboratories.

IWGACP recognizes that analysts need to be rigorously trained in mineral characterization, with emphasis on analysis of cosmetics for asbestos contamination, to provide adequate confidence in the proficiency of the analysts and the laboratory, and the reliability of the data.

Mineral characterization is a complex discipline and requires a high degree of technical skill and competence. Therefore, IWGACP considers the following to be critical for performing reliable analysis of cosmetics for asbestos:

[26] Docket FDA-2020-N-0025 located at https://www.regulations.gov/docket/FDA-2020-N-0025.

i. The analysts should have received formal training in mineral identification and determination of asbestos, as well as in the instrumentation and methods required for the analysis.

ii. A quality management system, such as that described in ISO 10012:2003 (Measurement Management Systems – Requirements for Measurement Processes and Measuring Equipment) and ISO/IEC 17025:2017 (General Requirements for the Competence of Testing and Calibration Laboratories) should exist.

iii. Analysts who have routinely followed published methods [27] regarding the measurement of asbestos in materials should preferably be testing talc-containing cosmetics for asbestos. Many of these methods were written for determination of asbestos in airborne particles or bulk materials; laboratories tasked with analyzing for low levels of asbestos in cosmetic talc products have had substantial success adapting these methods. Analysts should have additional, documented training in analysis of low-level asbestos samples.

iv. Bulk materials are tested for asbestos by analysts who have demonstrated proficiency using well-characterized materials,[28] and programs are in place for accreditation of laboratories performing such testing by third-party organizations.[29] IWGACP advises that an analogous approach should be developed and followed for testing of cosmetics for asbestos.

2. Summary

In summary, the IWGACP recognizes that a high degree of skill is required for reliable mineral characterization in the analysis of cosmetics for asbestos. IWGACP encourages the continued practice of employing skilled professionals who receive periodic training in testing for asbestos, and the incorporation of proficiency testing and accreditation programs into the laboratory quality management systems. IWGACP advises that training, proficiency testing, quality

[27] Methods such as: ISO 10312:2019 (Ambient Air - Determination of Asbestos Fibres – Direct Transfer Transmission Electron Microscopy Method); ISO 13794:2019 (Ambient Air - Determination of Asbestos Fibres – Indirect-Transfer Transmission Electron Microscopy Method); ASTM D6281-15 (Standard Test Method for Airborne Asbestos Concentration in Ambient and Indoor Atmospheres as Determined by Transmission Electron Microscopy Direct Transfer Method); EPA/600/R-93/116 1993 (Method for the Determination of Asbestos in Bulk Building Materials); EPA/600/R-94/134 100.2 1994 (Determination of asbestos structures over 10 μm in length in drinking water); 40 CFR Part 763 A-D Subpart E AHERA; OSHA 1901:1001 (Polarized Light Microscopy of Asbestos); OSHA ID160 (Asbestos in Air. July 1988); NIOSH method 9002 (Asbestos (bulk) by PLM); NIOSH method 7400 (Asbestos by TEM).

[28] Samples of asbestos and other minerals are available from commercial sources such as Research Triangle Institute, AIHA, and U.S. government labs, such as USGS and NIST.

[29] Organizations that accredit a laboratory for measurement of asbestos include, but are not limited to, NIST National Voluntary Laboratory Accreditation Program (NVLAP), American Industrial Hygiene Association's Laboratory Accreditation Program (AIHA-LAP), and The NELAC Institute (TNI) (National Environmental Laboratory Accreditation Conference).

management, and independent oversight are essential elements of a standardized approach to testing cosmetics for asbestos.

APPENDIX I: SAMPLING AND SAMPLE HANDLING

This section contains the outcome of the deliberations among scientific experts in the IWGACP regarding sampling and handling analysis of asbestos in talc and talc-containing cosmetics to overcome the issues of asbestos inhomogeneity in talc and cross-contamination affecting trace asbestos analysis. These scientific opinions and related advice do not represent recommendations or policies of the FDA or any other federal agency.

Procedures for sampling and sample handling should include measures to minimize cross-contamination. There are numerous standard methods for sampling and handling other asbestos-containing materials, such as building materials, that are often applicable, in part, to the topic at hand and are referenced in the following sections. Enough sample should be collected to allow for complete analysis by all methods and to provide for an archived sample should additional testing be necessary.

1. Sampling

Each of the regulatory agencies contributing to the IWGACP has their own written procedures for taking samples that are formulated based on risk. The FDA has written procedures for sampling articles in domestic commerce such as talc and cosmetics. Written modifications can be made to these general procedures on a case-by-case basis as needed, e.g., to mitigate risk of contamination or obtain representative samples. The public can view FDA's procedures by consulting the FDA Regulatory Procedures Manual.[30] However, it is important to note that FDA procedures for taking compliance actions only require sampling a minimum number of units and generally assume homogeneity, i.e., the procedures cannot readily account for unknown inhomogeneity with respect to the analyte in the product.

IWGACP advises that persons seeking to obtain representative sample in talc-containing cosmetic products consider applying what is known about the homogeneity of the analyte in the product.

Public standard methods and general guidelines provide statistically valid approaches for obtaining representative samples from bulk materials [USP General Chapter <1097>; ISO 14488:2007; ISO 11648-1:2003; ISO 11648-2:2001; ISO 10725:2000(E)] which may be suitable for sampling of talc and consumer products containing talc for asbestos. Petersen *et al*. (2005)

[30] See https://www.fda.gov/inspections-compliance-enforcement-and-criminal-investigations/compliance-manuals/regulatory-procedures-manual.

provide a good explanation of the theory of sampling with regards to heterogeneous (solid) materials with practical applications.

The IWGACP's scientific opinion, given the small amount of sample that will be tested, is that samples taken for microscopic analysis represent the distribution of asbestos and other amphibole mineral particles in the batch, or lot, from which the product is produced. The sampling strategy should consider information about the extent of variability in the individual samples or subsamples that collectively would be termed as "representative" of the original batch or lot. With respect to combining individual samples prior to testing, composite samples should not mask a defect that otherwise would be detected by testing the individual sample.

Mineral particles are often non-homogenously distributed in talc and talc-containing cosmetics. Individual subsamples may be analyzed separately or combined to make a composite that statistically represents the overall composition of the sample. The compositing of subsamples is not recommended unless and until verification shows that the specific compositing method does not compromise the limit of detection. Of particular concern is that compositing a subsample that contains a high level of asbestos with subsamples that have non-detectable or low levels of asbestos could dilute a potentially violative subsample and result in non-detection, even though asbestos is present in the cosmetic product.

Given differences in particle shape and size among elongate mineral particles and other components in powders that comprise products and blends used to fabricate products, the IWGACP finds that it is important to consider the potential for segregation resulting in areas being sampled that might have relatively high concentrations (or low) compared with other areas being sampled. In addition, minerals such as talc would not necessarily contain equal concentrations of amphibole and serpentine minerals. The EPA confronted the non-homogenous distribution of asbestos in, or on, the soils at Superfund sites. The EPA used an incremental sampling scheme that combines many samples into a single composite sample that represents the average soil contamination (Wroble *et al*., 2017; Pooler *et al*., 2018; Interstate Technology & Regulatory Council). While this approach is not specified for talc or talc-containing products including cosmetics, it warrants consideration as a valid methodological approach.

2. Sample Preparation.

The primary goals of sample preparation for analyzing talc and talc-containing cosmetic samples for asbestos are to obtain a sample that is (a) representative, and (b) free of interfering substances (e.g., organic material or minerals such as carbonates). The IWGACP identified four major issues in sample preparation: (i) erratic distribution of asbestos particles in talc may lead to inconsistent and erroneous results and the analyst should make every reasonable attempt to obtain a representative samples for analysis; (ii) moisture and organic compounds in the sample can lead to inaccurate weight-based estimations of asbestos content; (iii) moisture and organic

compounds can also may interfere with the analyses, especially in microscopic methods (e.g., PLM and TEM); (iv) the sample may contain minerals that interfere with analysis and dilute the analyte, and may be removed by acid dissolution (e.g., carbonates).

The IWGACP considered four types of analytical approaches to detect mineral particles: XRD, PLM, TEM, SEM. Each method requires preparing separate aliquots from the same sample. Aliquots for XRD would most likely be pulverized to make a powder, while aliquots for PLM, TEM, and SEM should remain unground or un-milled to retain original particle dimensions and shapes. Aliquots supplied for PLM, TEM, and SEM should be of sufficient mass to allow replicate analyses and archiving. Laboratories should ensure the sample preparation methods have negligible effects on the dimensions of any particles present.

Regardless of the sample preparation method (e.g., removing moisture and organics, mixing/homogenization, dissolution), any change in sample weight between each of the steps in the procedure must be measured and recorded (weight accountability). Standard gravimetric procedures for preparing other bulk materials for asbestos analysis by optical and electron microscopy may be applicable and should be consulted when using gravimetric procedures to prepare talc and talc-containing cosmetic samples (e.g., ISO 11358-1:2014; ISO/IEC 17025:2017; ASTM E2402-11 (2017); CTFA E36-1; ASTM E11131-20; USP<731>; USP<733>). Thermogravimetic analysis can provide additional information on sample composition and volatile content (Mackenzie and Caillere, 1975; Jozanikohan et al. 2015).

3. Obtaining a Homogenous Sample and a Representative Aliquot for Analysis:

The distribution of asbestos in talc samples is often heterogenous, and therefore the sample should be mixed and homogenized to obtain a representative analytical aliquot. Historical means of homogenization include but are not limited to tumblers, vibrators, sonication, ball milling, cone-and-quartering, and manual mixing. Gentler three-dimensional mixing devices (e.g., V-tumblers) have been used and are recommended in some procedures (e.g., California EPA 1991); however, the IWGACP could not find published validated methods using these mixing devices (e.g., ISO, ASTM) and encourages the analytical laboratory report the effect of each mixing method on particle size.

Many of the milling and vigorous mixing techniques (e.g., ball milling) have been used for asbestos-containing bulk materials, such as construction materials, in which particle size is coarse compared to cosmetic talc. The IWGACP advises that these methods *not* be used for talc-containing cosmetic products which contains fine sized particles, since such methods could result in further mineral particle breakage and fragmentation (Assuncao and Corn, 1975; Langer et al. 1978; Salamatipour et al. 2016).

A variety of methods for splitting the sample or making a sample composite may be suitable for talc-containing cosmetics. These include riffle splitters, rotary splitters, and cone-and-quartering; however, precautions should be taken to ensure that particle sizes and shapes are not altered (USP<1097>, USBM IC 9431).

4. Archiving

IWGACP advises that all samples be retained for a period of time sufficient to ensure opportunity for the laboratory to perform repeat testing, and for other laboratories to attempt to replicate findings. The IWGACP advises FDA to provide guidance related to the specifications for sample archiving.

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APPENDIX J: SAMPLE PREPARATION METHODS: SEPARATION AND CONCENTRATION OF ASBESTOS FROM OTHER MINERALS, INCLUDING TALC

1. Overview/Summary

This section contains additional information on the IWGACP's opinions regarding sample preparation methods for analysis of asbestos in talc and talc-containing cosmetics. These scientific opinions and related advice do not represent recommendations or policies of the FDA or any other federal agency.

Certain methods have been explored for their capacity to separate amphibole and chrysotile asbestos from talc. Some of these methods (e.g., ashing, acid dissolution) have been used successfully, reducing materials that interfere with asbestos analysis. Other methods (e.g., density centrifugation) have been explored for separation of asbestos from other minerals, however, these methods have not been validated.

Several methods have been described for the separation of small amounts of asbestos minerals from talc. Some common methods for industrial talc preparation or laboratory-scale separation involve fluid (liquid or gas)-based separation taking advantage of differences in apparent density (or other characteristics) of mineral particles. The methods include sedimentation in water (elutriation), froth flotation, air elutriation, and density centrifugation. Some of these approaches are promising for analytical laboratory separation of minor levels of asbestos from talc or talc-containing cosmetics for quantification. Their continued development for isolation of low levels of asbestos in talc is *strongly* encouraged. When any method is used to separate asbestos from talc and asbestos is detected, there can be reasonable assurance that asbestos was present in the original sample (qualitative measurement); however, when any asbestos separation methods are used and no asbestos is detected, unless the efficiency of the method has been confirmed for each mineral and particle size, one cannot conclude asbestos is not present. Analytical laboratories and regulatory agencies would benefit from development of efficient methods for separation of low levels of asbestos from talc for quantitative measurements.

2. Purpose

The purpose of this appendix is to provide background information and analysis of some of the methods used for the separation of minerals (e.g., asbestos), from other accompanying minerals (e.g., talc).

Types of Methods Needed

The sensitivity of an analytical method is enhanced when sample preparation methods are used to isolate and concentrate the analyte of interest. When a target analyte (i.e., asbestos) is a minor component of a sample matrix (i.e., talc or talc-containing cosmetic), the analytical sensitivity is enhanced by the removal of non-target materials in the sample matrix, especially those that would interfere with target analyte detection. Examples of this are removal of carbonates with acid or removal of organics by heating (i.e., ashing). Similarly, if the target analyte occurs non-uniformly in the sample matrix, concentration of the target analyte from a large amount of sample ameliorates the impact of non-homogeneity. Many sample treatment methods are useful at different stages of analysis, depending on the questions that are being asked (e.g., fit-for-purpose). Some methods are designed to answer qualitative questions (i.e., is the target analyte present; 'yes' *vs* 'no') while others are designed to answer quantitative questions (i.e., how much target analyte is present in the sample).

3. Ashing and Acid-Based Dissolution

The most common approach that removes interfering substances during talc or cosmetic sample preparation involves ashing (also known as muffle furnace ignition) followed by dissolution of the residue with hydrochloric acid. Ashing removes moisture and organic matter, whereas the acid treatment removes acid-soluble minerals (e.g., magnesite, calcite, dolomite, and chlorite) which may be present in talc. This approach has been described in written protocols for building materials containing at least 1% asbestos (e.g., NY ELAP methods 198.4 and 198.6; EPA 600/R-93/116); however, this approach also appears to be effective for analyzing talc samples containing <1% asbestos.

The IWGACP advises that temperatures used during ashing should not exceed 480˚C and that the ashing device (e.g., furnace) should maintain the temperature to within a few degrees. Thermal analysis data in published literature suggest that heating to 480˚C has no effect on the chemical or physical properties of amphibole and serpentine mineral particles or talc, whereas temperatures above 500˚C affect chrysotile structure (EPA/600/R-93/116). Thermogravimetric analysis (TGA) can be used to determine the effects of heating on weight (inferring composition) of samples (Mackenzie and Caillere, 1975; Jozanikohan et al. 2015).

The quantitative isolation of the target analytes (i.e., asbestos particles) from the non-target materials (i.e., organic material, carbonates, chlorites, and talc) should be a primary goal of analytical laboratories. The gravimetric reduction methods (e.g., ashing, acid digestion) afford some concentration of target analyte particles by removing the removal of organics and carbonates. Promising alternative methods for removing interfering substances have been used for the detection of asbestos in building materials or soils (non-talc) and include sedimentation, float-sink methods in water or organic liquids, differential density separation using heavy liquids

(with or without centrifugation), solvent/fluid separation (Addison and Davies, 1990), use of fluidized bed asbestos segregation (e.g., FBAS, soils), aqueous elutriation, acid-base refluxing, and wet sieving. Some of these methods may be beneficial for analysis of talc-containing cosmetics when used in addition to the gravimetric reduction methods. Accuracy and reliability have been demonstrated in interlaboratory studies for some of these methods, for certain matrices, but not necessarily for talc-containing cosmetics. [ISO 22262-1:2012; ISO 22262-2:2014; ASTM D7626-19; ASTM D7521-16; Addison and Davies, 1990; EPA 2018; Januch et al. 2013; Farcas et al. 2017; Wroble et al. 2017; Wright and O'Brien, 2007; Webber et al. 2004; Webber et al. 2008; Pier, 2011; Pier and Ferret 2013; New York Environmental Laboratory PLM method ELAP 198.8 (2016); Peters and Smith, EPA/600/2-80/172; EPA 1993 (EPA/600/R-93/116)].

4. Water Sedimentation, Flotation, and Elutriation of Asbestos

Sedimentation:

The sedimentation rate of solids in water is dependent on the specific gravity of the solid, water characteristics (viscosity, sediment load, temperature, turbulence, flow), and hydrodynamic (similar to aerodynamic) characteristics of the solid particles (Hanna *et al*., 1982).

Webber *et al.* (2008) described the application of a water column method to isolate (elutriate) the various size fractions of amphiboles (tremolite, winchite, richterite) that were present in vermiculite mined in Libby, Montana. They used the USGS Libby 6-mix (Lowers *et al.,* 2012) and elutriated fractions (<2.5 µm and >2.5 µm in length), with 2.5 µm being upper limit of particles with aerodynamic diameter consistent with respiratory alveolar exposure (Webber *et al.,* 2008). The Libby 6-mix was applied to a water column and provided a vertical flow to allow particles >2.5 µm in length to settle and those <2.5 µm in length to flow upward and be collected. This approach by Webber *et al*. has been used to elutriate <2.5 µm asbestos fractions from various mineral sources and determine the size-dependent toxicity of these asbestos minerals (e.g., Duncan *et al*., 2010; Padilla-Carlin *et al*., 2011; Cyphert *et al*., 2012, 2015, 2016).

Toland (2000; Sections 9.22-9.26) detail the elutriation process including wetting and submerging exfoliated[31] vermiculite in water and allowing asbestos and other minerals denser than exfoliated vermiculite to disperse and settle in the water. A refinement of this method is described in the EPA research method EPA/600/R04/004 (EPA, 2004) for the isolation of asbestos from vermiculite attic insulation and lists a sensitivity of 0.01% by weight.

Froth Flotation:

Froth flotation is an elutriation method widely used in industry to both concentrate valuable minerals from ores (e.g., concentrating gold-bearing sulfides from host rock), and to remove

[31] Exfoliated by expanding with water and heat (Toland, 2000; Hillier et al., 2013).

undesirable components from materials (e.g., separating sulfide minerals from coal or removing contaminants in environmental cleanup processes) (see Nguyen and Schultze (2003), Polat *et al*. (2003), and Galvin (2006). Two of the major types of froth flotation are mechanical and column.

Mechanical Froth Flotation: Mechanical froth flotation is an elutriation method performed in a vessel with a high-shear impellor to mix air and slurry and cause air bubbles to collide and attach to hydrophobic particles. The bubble carries the particle to the surface where it is collected in a froth (Nguyen *et al*., 2004; Polat *et al*., 2003; Galvin, 2006). This approach has not been described as a promising method for separation of low levels of asbestos from talc (Patra, 2011).

Column Froth Flotation: Column froth flotation is an alternative to mechanical froth flotation and is a more quiescent elutriation technique which was introduced to ore processing in the 1960's (Finch 1995; Sastri, 1998). Column flotation has been used in industry for beneficiation of talc ore resulting in significant increases in the purity of the talc to approximately 90% (Kho and Sohn, 1989; Feng and Aldrich, 2004; El-Rahiem, 2005; Kursun and Ulusoy, 2006; Kursun and Ates, 2010; Divya et al., 2017).

The process utilizes a tall column of water where fine bubbles are introduced near the bottom of the column and the mineral slurry is introduced along the column height. The bubbles selectively attach to the hydrophobic mineral particles (e.g., talc) causing them to rise to the top while the hydrophilic particles (e.g., asbestos) settle to the bottom. This method is optimized for specific ores by variations in the column equipment and flotation reagents used (Kursun and Ates, 2010; Kursun, 2011; Divya *et al*., 2017).

Despite the numerous methods and publications on beneficiation of talc and other minerals, the IWGACP did not find publications detailing qualitative or quantitative methods for aqueous elutriation or froth flotation to separate small amounts of asbestos mineral particles from talc or talc-containing cosmetics for quantitative analysis.

5. Fluidized Bed Asbestos Separation (FBAS)

Spurny *et al.* (1979) described the use of a vibrating bed aerosol generator where they had experimented with the optimum vibration frequency and amplitude in the dissociation of different sizes of asbestos fibers from bundles in asbestos samples. With this approach, they were able to separate asbestos into multiple size fractions, and then further use aqueous sedimentation to achieve additional separation and accumulation of enough asbestos mass for testing (Spurny *et al.* 1979).

The EPA published a method in 1997, using in-part the work of Spurny et al (1979), on the testing of Superfund sites for the presence of asbestos in releasable dust from the soil (EPA,

1997). In this method, soil samples are tumbled in a vessel and the released dust is removed with a gas flow and collected on sample filters for weighing and TEM analysis. The dust generator used in this method (Berman elutriator) was complex and required a lot of time to decontaminate between samples resulting in a relatively low throughput (number of samples per day). To the best of our knowledge, this method (Berman elutriator) has not been subjected to interlaboratory testing.

The EPA started investigating the utility of a fluidized bed asbestos segregator (FBAS) in 2007 as a technique for identifying and quantifying mineral fibers present in soil or other solid media such as vermiculite (Januch *et al*., 2013; EPA, 2018). The EPA and Battelle Energy Alliance, LLC., under contract with the Idaho National Laboratory (INL) developed an advanced method using air-elutriation to preferentially elutriate asbestos fibers from vibrating soil (Januch *et al.,* 2013). The FBAS is used as a sample preparation instrument that utilizes air elutriation to separate light weight asbestos structures from heavier matrix particles and deposit these structures onto a filter which can then be analysed by TEM (with EDS and SAED) or another appropriate microscopy method.

Details of the FBS method are presented in Januch *et al.* (2013) and EPA (2018). In brief, soil samples are thoroughly dried, sieved to remove larger particles, combined 1:20 – 3:20 with laboratory-grade sand, and air is drawn through the sample/sand mixture while the mixture is vibrated mechanically. Fractions of the airborne particles are collected on mixed cellulose ester (MCE) or polycarbonate filters and analyzed by TEM or SEM. The air filter is typically analyzed by TEM for asbestos in basic accordance with the recording rules specified in method ISO 10312.

The EPA has conducted several studies with soil to evaluate the performance of the FBAS method in determining asbestos contamination. In Januch *et al.* (2013), performance evaluation (PE) standards were prepared with asbestos-free soils from Durham County North Carolina, spiked with 0.0001–0.1% chrysotile asbestos, or uncontaminated soil from Arvada, Colorado, spiked with known levels of amphibole asbestos (0.0001–0.1%; primarily winchite, richterite and tremolite) from the Libby Asbestos Superfund Site in Libby (see **Figure J-1**). The study also evaluated the performance of the FBAS using vermiculite attic insulation spiked with chrysotile or tremolite asbestos at 0.0001–0.1% by mass. Januch *et al.* (2013) were able to achieve detection limits of 0.002–0.005% asbestos by weight for the spiked soil and vermiculite samples. The authors noted "… *there is relatively high variability between replicate filter analyses. It appears that the most important source of this variability is random Poisson counting variability during filter analysis by TEM*." (Januch *et al.,* 2013).

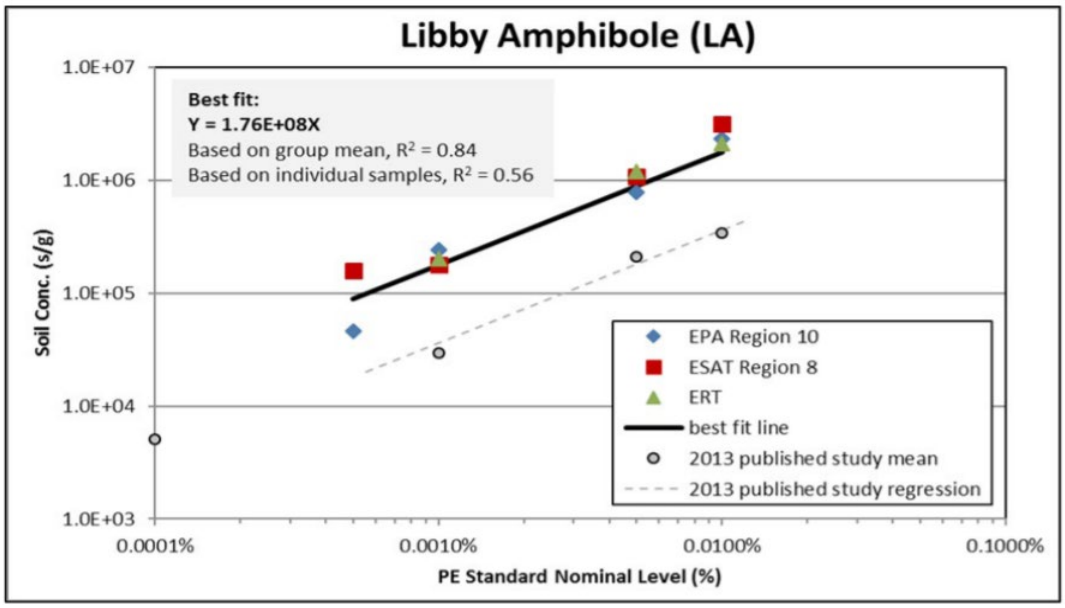

Figure 8 – PE sample results – Average Libby Amphibole Results from 2011 and 2015 studies.

Figure J-1. The PE sample analysis results using FBAS (Figure 8 from EPA 2018).

Several other studies have used the FBAS method to successfully analyze asbestos in soils, including soils from the Slim Buttes area (Custer–Gallatin National Forest, South Dakota; Farcas et al., 2017) and Sumas Mountain, Washington (Wroble et al., 2017).

The EPA publication of analytical methods[32] describes FBAS method OTM-42 (EPA, 2018) which involved a three-laboratory, interlaboratory validation study conducted in 2015 that used PE standards consisting of uncontaminated Arvada, Colorado, soil containing either fibrous Libby amphibole structures, amosite asbestos, or chrysotile asbestos at concentrations of 0.01%, 0.005%, 0.001% and 0.0005% by weight. This 2015 study illustrates an approximate linear relationship between the nominal concentration of asbestos in the PE standard and the concentration estimated by TEM analysis expressed as asbestos structures per gram of test material (s/g). The method detection limits of each in this study fell within 0.002% to 0.003% by weight.

In a study by Berry *et al.* (2019), uncontaminated Arvada, Colorado, soil was spiked with 0.0001–0.1% erionite from Rome, Oregon. The authors also tested two field samples (Dunn County, North Dakota; Custer National Forest, Montana) that were taken from areas where erionite is present in soils. The samples were elutriated using the FBAS method, and samples were analysed by TEM following ISO 10312 protocol. The authors demonstrated a linearity (r^2

[32] The EPA Air Emission Measurement Center (EMC) publishes a list of new methods which have not yet been subject to the Federal rulemaking process in an "Other Test Method" document (OTM; EPA 2018).

of 0.93 for group means) between 0.001–0.1% spiked samples. The authors noted a minimum detection limit of 0.003% for FBAS+TEM when the probability of detection of erionite on sample filters is set at 80%.

To date, however, there have been no published studies investigating the use of the FBAS method for determining the asbestos content in talc. Talc presents some unique problems that are not present in soils, such as, (*a*) the similarity of density (g/cm^3) for talc and some asbestos amphibole minerals, and (*b*) the fine particle size of cosmetic talc.

6. Heavy Liquid Separation (HLS) of Minerals

HLS is a mineral separation method that uses (*a*) high density liquids (>2 g/cm^3) and (*b*) centrifugation to separate minerals (i.e., asbestos from vermiculite). HLS is a published method for the separation of asbestos from vermiculite building materials and is mentioned in the ISO 22262-2 standard (sec. 16); however, there are currently no published HLS methods for separation of asbestos particles from talc.

The use of HLS for separating minerals of different density has been discussed in academic and industrial circles since the 1800s. Many of the heavy liquid solutions used in today's laboratories were developed in the late 1800s and early 1900s, including Klein's[33] and Clerici's[34] solutions. HLS is taught as a basic practice in mineralogy, geology, and geological science courses across the world, the solutions are widely available, and the technique has been used by commercial laboratories for mineral separation.[35]

This method has been used for a long time, as illustrated by Rosenblum et al. (1974) where it is stated that Clerici's solution *"... has been in use at least 65 yr for separation of minerals containing tin, chromium, niobium-tantalum, the rare-earth metals, and so forth from 'medium-heavy' minerals (density between 2.85 and 3.30) by investigators ..."*. The United States Geological Survey (USGS) published a document on the safe handling of heavy liquids for the separation of minerals during sample preparation (Hauff and Airey, 1980). In the circular,

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[33] Klein's solution: Cadmium borotungstate (CAS 1306-26-9) has a maximum specific gravity of 3.28 g/cm^3 at 15 °C [The magnetitic concentration of iron ore, Discussions held at the Glen Summit meeting, October 1891. Transactions of the American Mining Engineers, volume 20, pp. 582. 1892; Hussak, E. II, Klein's Solution. IN: E. Hussak, The Determination of Rock-forming Minerals. pp.73-75. 1896].

[34] Clerici's solution: aqueous solution of equal parts of thallium formate (CAS 992-98-3) and thallium malonate (CAS 2757-18-8). A saturated solution (500 g each salt in 100 mL water) has density of 4.28 g/cm^3 at 20 °C (4.25 g/cm^3 at 15 °C) [Clerici, E. 1907. Preparazione di liquidi per la separazione dei minerali. Atti. R.A. Lincei, Rome. 16, 187-195; Vassar H.E. 1925. Clerici solution for mineral separation by gravity. American Mineralogist 10(5), 123-125; https://www.mindat.org/glossary/Clerici_solution].

[35] Partial list of companies conducting HLS analysis: https://www.chem.com.au/heavy_liquid.html; https://www.heavyliquids.com/techdata.html; https://www.alsglobal.com/en-us/services-and-products/metallurgy/exploration-and-brownfields-studies/heavy-liquid-separation; https://sites.google.com/site/concentrationofminerals/home.

USGS states that *"… the heavy liquids bromoform ($CHBr_3$), methylene iodide (CH_2I_2), tetrabromoethane $(CHBr_2)_2$, and Clerici compounds are organic chemicals of primary importance in the mineral separation processes followed in many geologic laboratories. For years geologists and their technicians have used and abused these highly toxic substances …".*

The Australian government has published a document on acceptable methods for separating and analysis of many mineral types (Chisholm *et al.,* 2014). The liquids that are mentioned for heavy (or dense) liquid gravity (or centrifugal) separation include: tetrabromoethane (CAS 79-27-6), 2.96 g/cm^3; diiodomethane (CAS 75-11-6), 3.3 g/cm^3; lithium heterotungstate[36], 2.86 g/cm^3; sodium polytungstate (CAS 12141-67-2), 2.9 g/cm^3. Chisholm *et al.* (2014) does not focus on asbestos; however, it does include practical procedures for the separation of minerals which could be applied to asbestos and talc.

The New Jersey Department of Environment Protection, Geological and Water Survey, published a series of technical reports on the use of heavy liquids in the separation of minerals for analysis of the mineral type (Grosz *et al.,* 1990; Uptegrove *et al.*, 1991, 2016). These reports have provided guidance for characterization of minerals within the state.

It is important to note that many of the liquids used HLS separation of minerals are toxic, as mentioned by Hauff and Airey (1980), Chisholm *et al*. (2014), Grosz *et al.* (1990), and Uptegrove *et al.* (1991, 2016), including Klein's solution [contains cadmium borotungstate (CAS 1306-26-9; $B_2Cd_5H_{36}O_{98}W_{24}$)][37], Clerici's solution [contains thallium formate ($C_4H_2O_6Tl_2$; CAS 992-98-3) [38] and thallium malonate ($C_3H_4O_4Tl$; CAS 2757-18-8)] [39, 40] bromoform ($CHBr_3$; CAS 75-25-2) [41], methylene iodide (CH_2I_2; *a.k.a.* diiodomethane; CAS 75-11-6) [42], tetrabromoethane ($(CHBr_2)_2$; 1,1,2,2-tetrabromoethane; CAS 79-27-6) [43], lithium

[36] No CAS was provided for this chemical. This may refer to the high density aqueous polytungstate (metatungstate) solutions of lithium tungstate which achieve densities of 2.86 g/cm^3 at 25 ºC to 3.3 g/cm^3 near 100 ºC.
[37] Cadmium borotungstate MSDS sheet at https://www.pfaltzandbauer.com/SDSFile.ashx?ItemCode=C00120 ; cadmium toxicity is well known, see https://www.cdc.gov/niosh/topics/Cadmium/.
[38] Thallium formate toxic profile. https://echa.europa.eu/substance-information/-/substanceinfo/100.012.363.
[39] MSDS sheet for thallium malonate indicates same toxicities as thallium formate (http://www.acros.com/Ecommerce/msds.aspx?Language=en&PrdNr=42079).
[40] Thallium compound toxicity; https://cfpub.epa.gov/ncea/iris/iris_documents/documents/toxreviews/1012tr.pdf ; https://rais.ornl.gov/tox/profiles/thallium_f_V1.html.
[41] Bromoform toxicity profiled at https://19january2017snapshot.epa.gov/sites/production/files/2016-09/documents/bromoform.pdf.
[42] Methylene iodide toxicity; https://www.fishersci.com/store/msds?partNumber=AC169830250&productDescription=DIIODOMETHANE%2C+99%2B%25+25GR&vendorId=VN00032119&countryCode=US&language=en.
[43] Tetrabromoethane toxicity; http://datasheets.scbt.com/sc-237646.pdf.

heteropolytungstate;[44,45] and sodium polytungstate ($H_2Na_6O_{40}W_{12}$; CAS 12141-67-2).[46]

7. Heavy Liquid Separation of Asbestos from Other Minerals

Apparently, the talc industry was aware in the early-1970s of the possible application of HLS for isolating and concentrating asbestos from talc samples as a method of improving analytical sensitivity. The Johnson & Johnson Company contracted F.D. Pooley (University of Cardiff, Wales, UK) in 1973 to conduct an evaluation of the use of HLS to separate amphibole minerals that may be present in talc (Johnson & Johnson, 1973). Pooley's publication describes HLS technique using a mixture of 1,1,2,2-tetrabromoethane (CAS 79-27-6; 2.97 g/cm^3 at 20 ºC) and toluene (CAS 108-88-3; 0.87 g/cm^3 at 20 ºC) in a 17:1 mixture to achieve density of 2.83 g/cm^3 at 25 ºC or at a 7:1 mixture to achieve a density of 2.68 g/cm^3 at 25 ºC. The minerals were collected on glass fiber filters after centrifugation. Although no details of analysis were provided, the publication provided indication of the effectiveness of the separation.

R.P. Bagioni (1975) also described the separation of asbestos from other minerals using HLS techniques with organic fluids of specified densities. Samples of mixtures of amphibole, talc, serpentine and phyllite were suspended in 3 mL of 1,1,2,2-tetrabromoethane:carbon tetrachloride[47] (35:15; density 2.45-2.50 g/mL at 20ºC), quantitatively transferred with 2 mL of the 1,1,2,2-tetrabromoethane:carbon tetrachloride (35:15) solution, and centrifuged at 2000-2500 rpm.[48] The authors stated the asbestos minerals were collected by filtration through 0.45 µm Millipore filters (type HA). The collected asbestos fibers were then detected using infrared spectrum analysis of the -OH bond stretch at 3670 cm^{-1}. The ability of this method to separate and concentrate the asbestos fibers was clearly demonstrated.

Haartz *et al.* (1978) used bromoform (CAS 75-25-2; 2.89 g/cm^3) and tetrabromoethane (CAS 79-27-6; 2.97 g/cm^3) for HLS separation of tremolite, cummingtonite and grunerite from quartz, micas and other silicates. No additional information was provided regarding the density of the bromoform and tetrabromoethane solution, or the ability of the density-based separation method to concentrate asbestos fibers.

Addison and Davies (1990) commented that "… *a number of methods of concentrating amphibole contaminants and separating them from a matrix of chrysotile were considered, including froth flotation (Ralston and Kitchener, 1974) and heavy liquid separation ... but these*

[44] No CAS was provided for this chemical. This refers to the high density aqueous polytungstate (metatungstate) solutions of lithium tungstate which achieve densities of 2.86 g/cm^3 at 25 ºC to 3.3 g/cm^3 near 100 ºC.
[45] Lithium heteropolytungstate toxicity: https://www.chem.com.au/heavy_liquid.html.
[46] Sodium polytungstate toxicity; http://www.molbase.com/en/msds_12141-67-2-moldata-70791.html.
[47] 1,1,2,2-tetrabromoethane (CAS 79-27-6) density of 2.97 g/cm^3; carbon tetrachloride (CAS 56-23-5) density of 1.59 g/cm^3.
[48] The centrifuge type and radius were not provided, so the speed (rpm) cannot be converted to force (*g*, units of gravity).

were found to be difficult to use routinely and were not quantitative." Furthermore, these authors indicated that caution should be used with some acid-based methods because "… *the magnesium could readily be leached by acids from chrysotile and that strong alkali could then be used to remove the remaining silica*." This analysis supports that inter-laboratory research on quantitative recovery should be conducted to understand the behavior of small levels of asbestos in talc and talc-containing cosmetics.

Blount (1991) used information from Tröger (1979) to generate a chart of the relative densities of talc, tremolite, anthophyllite, actinolite, cummingtonite and riebeckite (**Figure J-2**). Talc has a measured density ranging from 2.58-2.83 g/cm^3 (calculated density is 2.78 g/cm^3) [49] while tremolite, anthophyllite, actinolite, cummingtonite, and riebeckite have specific densities greater than 2.95 g/cm^3. On this basis, it would seem possible that if these minerals were suspended in a liquid of density between 2.85 and 2.95 g/cm^3, and subjected to sufficient centrifugation, the talc would rise to the top of the liquid while the tremolite, anthophyllite, actinolite, cummingtonite, and riebeckite would settle at the bottom of the liquid.

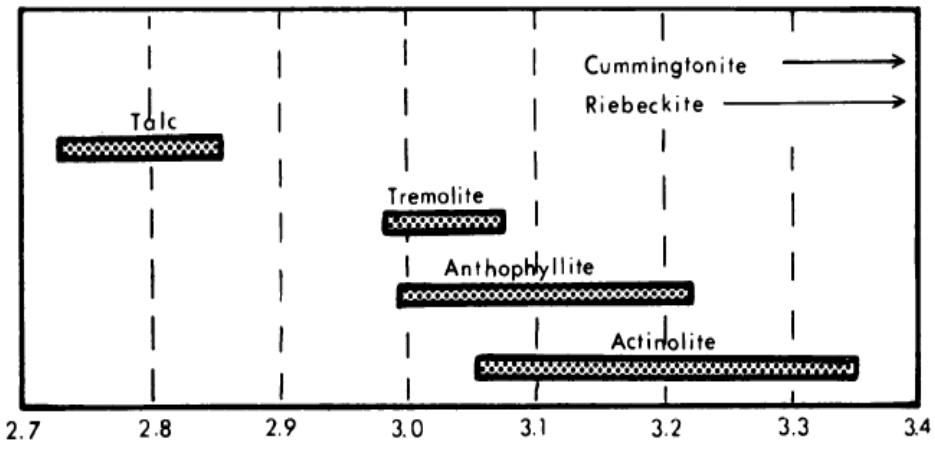

FIGURE 2. Specific gravities of talc and amphibole (6).

Figure J-2. Reproduced from Blount 1991 (reference #6 in figure is Tröger (1979)).

Blount (1991) used Klein's solution or Clerici's solution with specific gravity of 2.81 g/cm^3, and suspended talc containing 0.06%–1% tremolite (~60 mg) in 1.5 mL of the solutions. After degassing to remove air bubbles from the mineral particles,[50] the mixtures were centrifuged,[51]

[49] http://www.handbookofmineralogy.org/pdfs/talc.pdf.
[50] This is evidently a key step since air bubbles in tight association with the minerals, possibly interstitial air, would reduce their apparent density.
[51] The centrifuge head radius was not provided, so the speed (rpm) cannot be converted to force (*g*, units of gravity).

and the heavier particles recovered from the bottom of the tube for microscopic analysis. In comparing this method to the more typical method that does not remove interfering minerals, Blount concluded that the centrifugal concentration method gave the same results and provided approximately the same recovery when considering particle aspect ratio. The recovery and detection of tremolite at the 0.06% level was ~70% while the recovery and detection was ~90% at the higher levels of tremolite. The dense liquid separation described by Blount (1991) is mentioned in the mineralogy reference text by Petruk (2000).

The specific densities of talc and asbestos are presented in **Table J-1** and shown graphically in the **Figure J-3**. This figure illustrates that chrysotile has a density that is less than the density of talc, while the other asbestos minerals have densities greater than talc. This reinforces the comment "… *separation of chrysotile from talc by centrifugation in a heavy liquid is theoretically possible, in general it is not a practical technique*" (ISO 22262-2:2014). Actinolite, amosite, crocidolite and tremolite have densities (2.99-3.45 g/cm^3) that are above the range for talc (2.58-2.83 g/cm^3). The current information regarding the specific gravity of anthophyllite is a range of 2.85-3.57 g/cm^3, which differs from the data in Blount (1991) and Tröger (1979) with a range of 2.98-3.22 g/cm^3. More accurate determinations of anthophyllite density, or experimentally spiking talc with anthophyllite and isolating the anthophyllite using heavy liquid separation is required in order to understand the applicability of this method.

Table J-1. COMPILATION OF DENSITY OF ASBESTOS AND TALC

NAME	CAS NUMBER	SPECIFIC DENISTY, g/cm^3	SOURCE[52]
Chrysotile	12001-29-5	2.4-2.6	HSDB; https://pubchem.ncbi.nlm.nih.gov/source/hsdb/2966
Chrysotile	12001-29-5	2.4-2.6	ILO International Chemical Safety Cards (ICSC); http://www.ilo.org/dyn/icsc/showcard.display?p_version=2&p_card_id=0014
Chrysotile	12001-29-5	2.53	https://en.wikipedia.org/wiki/Chrysotile
TALC	**14807-96-6**	**2.58-2.83**	http://www.handbookofmineralogy.org/pdfs/talc.pdf
Anthophyllite	77536-67-5	2.9-3.5	http://www.handbookofmineralogy.org/pdfs/anthophyllite.pdf
Anthophyllite	77536-67-5	2.85-3.57	https://www.mindat.org/min-8738.html
Anthophyllite	77536-67-5	2.98-3.22	Blount (1991), Tröger (1979)
Tremolite	77536-68-6	2.99-3.03	http://www.handbookofmineralogy.org/pdfs/tremolite.pdf
Actinolite	77536-66-4	3.03-3.24	http://www.handbookofmineralogy.org/pdfs/actinolite.pdf ; https://www.mindat.org/min-18.html

[52] Many sources were consulted regarding the density of asbestos minerals and talc. The range of results from multiple data sources may provide the reader a sense of the consistency (or inconsistency) of the available information. Neither the inclusion of a particular source of information, nor the order of presentation, should be considered endorsement of the data source.

NAME	CAS NUMBER	SPECIFIC DENISTY, g/cm^3	SOURCE[52]
Crocidolite	12001-28-4	3.3-3.4	ICSC; http://www.ilo.org/dyn/icsc/showcard.display?p_version=2&p_card_id=1314
Amosite	12172-73-5	3.45	https://www.2spi.com/catalog/documents/Final_Asbestos-Amosite.pdf

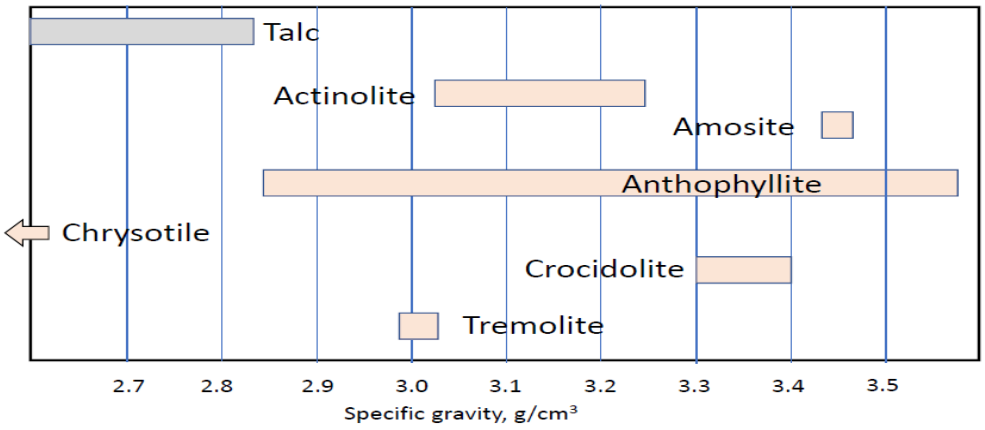

Figure J-3. Relative densities of the asbestos minerals and talc.

Toland (2000) describes in detail an HLS process for the determination of asbestos in vermiculite or vermiculite-containing products using aqueous sedimentation, and centrifugation in solutions of either 1,1,2,2-tetrabromoethane (CAS 79-27-6; 2.96 g/cm^3) or tribromomethane (bromoform; CAS 75-25-2; 2.89 g/cm^3) with the density adjusted to 2.75 g/cm^3 using ethanol. Toland (2000) included detailed description of the sedimentation velocities for various mineral sizes and length of centrifugation required to achieve equilibrium.

The International Standards Organization (ISO) describes methods for detecting and quantifying asbestos minerals in bulk materials in ISO 22262-2:2014, including detailed sections on a method for sample preparation by separation/concentration. In section 15.4 of the ISO standard, HLS (centrifugation) methodology is described for separation of amphiboles from a suspension of vermiculite using a preparation of lithium metatungstate solution with density of 2.75 g/cm^3 in a 15 ml centrifuge tube. Section 16 of ISO 22262-2:2014 indicates the HLS (centrifugation) method is also applicable to separation of amphiboles in talc using a liquid having a density of 2.85 g/cm^3; however, chrysotile may be more problematic to separate than the amphiboles because its density is similar to (or less than) the density of talc.

The New York State Department of Health method 198.8 recommends that the examination of vermiculite samples for the presence of asbestos include a step for separation and sedimentation of asbestos fibers from vermiculite using HLS in sodium polytungstate solutions (2.75 g/cm^3) (New York State Department of Health, 2016).

The use of new or modified techniques to isolate asbestos from other minerals has been a focus of many researchers over the past decade as evidenced by presentations and posters at the ASTM Johnson Conferences or ASTM Michael E. Beard Conferences. At the 2016 ASTM Michael E. Beard Conference on "*Asbestos and Fibrous Mineral Analysis and Research,*"[53] G. Tomaino gave a presentation on the use of HLS for isolating and detecting amphiboles and serpentines in pharmaceutical talc (Tomaino, 2016). At the 2017 ASTM Johnson Conference,[54] presentations were included on the effects of ultrasonication on asbestos (Saldivar and Burrelli, 2017), the use of FBAS to isolate asbestos (Januch *et al*., 2017), and concentration methods (Pier, 2017), along with a poster on HLS of OSHA archive talc samples (Mouldene, Asbestine, Nytal 99, Vanderbilt IT 325 and Nytal 100) in lithium metatungstate (2.95 g/cm^3) (Halterman (2017) as a follow-up to the work of Tomaino (2016). The author concluded that HLS analysis of talc using lithium metatungstate is promising, but that further research is required regarding the reliability of this method for detecting non-talc fractions of less than 1% from talc-based consumer products.

W. Longo testified to a U.S. House Subcommittee[55] that the use of HLS successfully isolates asbestos particles from talc, allowing greater sensitivity.[56] He additionally noted that HLS is not effective for concentration of chrysotile from talc due to similar densities.

As a result of these publications and presentations, it appears that both the mineral analytical industry and materials testing societies (e.g., ASTM) are aware of the use of HLS for isolating and possibly concentrating asbestos from other minerals, including talc, for quantitative analysis. The IWGACP notes there is a lack of published inter-laboratory qualitative and quantitative studies on the application of HLS to low-levels of asbestos in talc and talc-containing cosmetics.

DISCUSSION OF HLS

The IWGACP notes that HLS should be strongly considered as a candidate method in inter-laboratory studies for concentrating asbestos minerals from talc and talc-containing cosmetics. It

[53] 2016 Michael E. Beard Conference, https://www.astm.org/MEETINGS/SYMPOSIAPROGRAMS/D22ID2782.pdf.
[54] 2017 ASTM Johnson Conference, https://www.astm.org/MEETINGS/SYMPOSIAPROGRAMS/D22ID3216.pdf
[55] Hearing of the House Committee on Oversight and Reform, Subcommittee on Economic and Consumer Policy (11 Dec 2019).
[56] https://oversight.house.gov/legislation/hearings/examining-carcinogens-in-talc-and-the-best-methods-for-asbestos-detection.

is of particular concern that HLS is not able to separate chrysotile from talc because both minerals have similar densities.

IWGACP analysis of the literature points out two critical shortcomings of HLS to isolate and detect low-levels of asbestos in talc and talc-containing cosmetics:

> *(1)* The acceptance of the HLS technique for quantitative isolation of low levels of asbestos from talc requires inter-laboratory research to: *(a)* determine the reproducibility and accuracy of the method; (b) the effect of asbestos and other mineral particle size (length, width) on the recoveries from talc.
>
> *(2)* Talc standards (talc with specific levels of asbestos of known homogeneity, concentration, size, aspect ratio) do not exist and would be required for inter-laboratory comparisons of results using this method. Rohl and Langer (1974) described a process to generate standards with specific populations of asbestos minerals in talc; however, there are no commercially available talc-asbestos standards with specific asbestos minerals at concentrations below 1%.

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APPENDIX K:
CONTENT AND FORMAT OF ANALYTICAL REPORTS

1. Suggested Content of a Laboratory Report

This section contains additional information on the IWGACP opinions regarding the content and format of analytical reports for analysis of asbestos in talc and talc-containing cosmetics. These scientific opinions and related advice do not represent recommendations or policies of the FDA or any other federal agency.

The laboratory report is part of a complete record that documents the testing of talc or a talc-containing cosmetic product for asbestos. Laboratory reports should provide a detailed explanation of the findings for each sample analyzed that allows a determination of whether asbestos and other amphibole mineral particles are present. The laboratory report should support the determination, where applicable, of whether the product meets an established standard (e.g., the acceptance criterion in a specification). The report should contain a description of any deviations from the procedures, including their effect on the reliability of the data.

Although laboratory report content was not specified in any of the published asbestos testing standards that IWGACP reviewed, asbestos testing laboratory reports appear to typically contain the following information:

1. Sampling and sample handling prior to testing[57]

    a) Protocol for sample collection – method used for obtaining sample representing a production batch prior to product release or collection of a product from the market
    b) Protocol for sample preparation for delivery to laboratories (may include method for blinding the sample)
    c) Record of chain of custody – a complete record of all transfers of samples/subsamples from collection through final disposition[58]
        i) Original Chain-of-Custody, signed and dated by the laboratory
        ii) Original Shipping Documents (e.g., bills of lading)
        iii) Sample Log-in Sheet with cross-reference of client sample numbers to laboratory sample numbers

[57] If this is not performed by the testing laboratory, this is the responsibility of the organization submitting the sample to the laboratory (typically designated as the "client"). In this case, the client's record of sample preparation becomes part of the full record pertaining to the analysis of the sample.
[58] A record of chain of custody should be initiated by the client if the latter collects the sample and becomes part of the full record pertaining to the analysis of the sample.

iv) Photographs of samples in condition in which they were collected and in condition in which samples were received by the laboratory

2. Analytical Methodology (for each technique of analysis, e.g., PLM, XRD, TEM) described in adequate detail[59] to enable another laboratory to repeat/replicate the laboratory's analysis

a. Sample preparation in laboratory – detailed description of each step whereby sample received from the client is partitioned or subdivided or aliquots are taken for analysis, interfering substances are removed, dilutions are made; recording of weights and volumes measured during the preparation
b. All relevant instrument conditions, including level of magnification for microscopic analyses
c. For any quantities reported, citation or description of relevant protocols for counting involving either expression of a weight percent or a number of particles of any given type in a quantity of sample (as described in scientific opinion 1 for pertinent types)
    i. General approach to quantitation
        1. by PLM (e.g., visual estimate, point count)
        2. by TEM (e.g., number of structures counted)
    ii. Stopping rules for counting
        1. by PLM (e.g., number of slides to prepare and fields to view)
        2. by TEM (e.g., specified number of grid openings to view and/or mineral particles to report)
d. For determinations where the reported finding may be negative or none detected, the respective detection limits
e. Criteria used for mineral identification and classification into categories based on mineral type[60].
f. References to published methods for asbestos analysis (air or bulk samples) with detailed description and justification, as applicable, of modifications to methods intended for the analysis of air or certain types of bulk samples
g. Methods of estimation of dimensions of individual particles of asbestos and other amphibole minerals and calculation of particle aspect ratio

3. Tabulation listing each particle meeting the reporting criteria (as described in scientific opinions 1 and 2) and providing relevant information to characterize each particle. This tabulation usually cites a standard that was used to classify each detected particle by structure type as well as a mineral type and determine the length and width of each structure

[59] As much detail as possible should be provided, even if reference is made to written standards.
[60] Classification based on growth habit is discouraged.

4. Images, spectra, and diffraction patterns supporting identification of mineral particles, as applicable to each instrument used for characterization[61]

5. A record supporting that analytical instrumentation was operating within established control limits and parameters (e.g., equipment calibration, preventive maintenance of equipment, use of reference materials and standards, negative and positive controls, latest laboratory accreditation including analysts involved in accreditation) [62]

In addition, laboratories may include the following items in a laboratory report of talc or cosmetic products for asbestos.

1- A report of analysis, sometimes referred to as a "Certificate of Analysis" (CoA)
2- An explanation of how samples are stored (archived) securely if the samples may at a later date be considered "evidence"
3- A narrative summarizing overall findings
4- Narratives summarizing the findings of individual samples

2. Format for Presentation of Data in Laboratory Reports

In general, all laboratories that test for asbestos should tabulate the particles, as described in scientific opinions 1 and 2 on "count sheets", and also provide images, spectra, and diffraction patterns. The format for data presentation should facilitate an interpretation of the data and the ability to collate information over time if there is a need for additional sampling and testing to understand trends or to perform a retrospective analysis of the data.

An evaluation of data records of cosmetic samples tested for asbestos submitted to fulfill regulatory decisions about product safety indicate they generally include a combination of manually entered data (e.g., log and bench sheets filled in by analysts) and electronic records (e.g., images, charts, tables, and spreadsheets with embedded formulae used to calculate or estimate values such as aspect ratio or mass). A summary of data can be presented as a certificate of analysis (CoA).

To facilitate data review, tabulations of particles should also be provided in the form of an electronic deliverable, such as a workbook of spreadsheets. The electronic deliverable can also include figures such as scatter plots displaying the data obtained for length, width and aspect ratios of populations of detected particles. All microscope images, spectra and diffraction patterns should also be included in the electronic deliverable.

[61] Should be provided as an electronic deliverable.
[62] See requirements that must be followed to maintain laboratory accreditation. Laboratories also need to follow applicable State and Federal regulatory requirements.

IWGACP finds that it is useful for spreadsheets used to report data to include automating calculations. The U.S. Environmental Protection Agency website (https://www.epa.gov/superfund/asbestos-superfund-sites-technical-resources#nades) provides examples of spreadsheets that laboratories may use to record analytical data, automate calculations, and develop electronic deliverables for clients. These examples may serve as a reference when developing spreadsheets for talc and cosmetic products containing talc.

3. Data Interpretation

Data interpretation, as it pertains to health or risk assessment, is beyond the scope of this White Paper. Data interpretation involving quantitative estimates of asbestos and other amphiboles in talc and talc-containing cosmetics depends on sampling and testing methodology and may involve multiple measurements. As discussed previously, there are a number of uncertainties that raise concerns that quantification of asbestos and other amphibole mineral particles can be inaccurate and imprecise.

APPENDIX L:
IWGACP PARTICIPANTS

Interagency Working Group on Asbestos in Consumer Products (IWGACP) List of Participants		
Agency	**Participant**	**Title**
FDA	Jose A. Centeno, PhD, FRSC *	Director, Division of Biology, Chemistry, and Materials Science Center for Devices and Radiological Health (CDRH)-OSEL)
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FDA	Linda M. Katz MD, MPH	Director, OCAC; CFSAN
FDA	Michael A. McLaughlin PhD	Supervisory Chemist, Office of Regulatory Affairs (ORA) /ORS/OFFLO (Office of Food and Feed Laboratory Operations)
FDA	Stanley R. Milstein PhD	Consumer Safety Officer, OCAC, CFSAN
FDA	Gregory O. Noonan PhD	Director, Division of Bioanalytical Chemistry, Office of Regulatory Science (ORS), CFSAN
FDA	Anil K. Patri PhD	Chair, Nanotechnology Task Force; Director, Nanotechnology Core Facility, National Center for Toxicological Research, (NCTR)-ORA; FDA/OC (Office of the Commissioner)/OCS (Office of the Chief Scientist)/NCTR/OCD (Office of the Center Director)
FDA	S. Frank Platek, MS, FMSA *	Biologist, Trace Examination Section, Organic Chemistry Branch FDA Office of Regulatory Affairs (ORA) /ORS/OMPTSLO (Office of Medical Products and Tobacco and Specialty Laboratory Operations)/FCC (Forensic Chemistry Center)
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NIST	Hazel M. Richmond *	Program Manager, National Voluntary Laboratory Accreditation Program (NVLAP): Asbestos Fiber Analysis (PLM, TEM)
OSHA	Daniel T. Crane *	Physical Scientist, Division of Industrial Hygiene Chemistry, Salt Lake Technical Center
OSHA	Donald J. Halterman * Chair, Subgroup 1	Physical Scientist, Division of Industrial Hygiene Chemistry Salt Lake Technical Center
USGS	Bradley S. Van Gosen	Research Geologist

* No longer on IWGACP

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